INTRODUCTION

Trastuzumab therapy initiated since August 2000 in 25% of the Metastatic Breast Cancer (MBC) patients over-expressing HER2. The product is licenced in monotherapy for patients pre-treated with anthracyclines and taxanes, or associated with paclitaxel for patients who can not be pre-treated by anthracyclines. Trastuzumab is an anti-HER2 monoclonal antibody immunotherapy. The French Ministry of health funded the HER.ME.S study started in 2001 to evaluate the economic impact of a targeted therapy.

OBJECTIVES

To evaluate the economic impact of trastuzumab treatment in MBC and to determine the prediction level of the HER2 Extra-Cellular Domain (H-ECD) rate on the 2-months treatment response using correlations.

METHODS

HER.ME.S (HERceptin/Metastatique/Sein) Study :

A clinical, biochemical and pharmaco-economic study: Prospective and multicentric trial. Clinical data were collated on line by 11 centers : 7 AP-HP (public assistance and hospitals of Paris) and 4 CRLCC (regional centers of fight against cancer).

Table 1 : Four Protocols

<table>
<thead>
<tr>
<th>Designation</th>
<th>Treatment Schedule</th>
</tr>
</thead>
<tbody>
<tr>
<td>T1</td>
<td>-100%</td>
</tr>
<tr>
<td>T3</td>
<td>Between -100% and -30%</td>
</tr>
<tr>
<td>TP1</td>
<td>Between -30% and +20%</td>
</tr>
<tr>
<td>TP3</td>
<td>&gt; 20%</td>
</tr>
</tbody>
</table>

Only HER2 3s or 2+ and FISH+ patients received treatment

Time to recruitment is 36 months, and in theory the follow-up time is 2 years

The 2-months treatment response is evaluated according to RECIST criteria.

Table 2 : RECIST criteria

<table>
<thead>
<tr>
<th>Response</th>
<th>Evolution of the sum of the longest diameters of the target lesion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Complete</td>
<td>-100%</td>
</tr>
<tr>
<td>Partial</td>
<td>Between -100% and -30%</td>
</tr>
<tr>
<td>Stable</td>
<td>Between -30% and +20%</td>
</tr>
<tr>
<td>Progression</td>
<td>&gt; 20%</td>
</tr>
</tbody>
</table>

The 2-months response is compared to H-ECD level at baseline and after 2 months.

RESULTS

In a 3-years follow-up period, 120 patients were pre-included and 88 received trastuzumab treatment :

- Average age : 54 years [25-75].
- Median time to treatment: 30.3 weeks [25-35].

81 patients dropped out :

- 54 for progression,
- 12 for cardiac toxicities,
- 3 for neurological toxicities,
- 5 because of patient will,
- 5 for other reasons,
- 4 for death.

41 patients out of 88 died : 40 after progression and 1 after an infection.

Overall Survival : 60 weeks [48-80].

Time to Tumour Progression : 34 weeks [27-43].

ITT analysis: 62 patients received TP1, 25 TP3 and 1 T1. No statistically significant difference between TP1 and TP3.

Correlation analysis established on 27 patients : risk 2.2 times higher to have a 2-months progression response for patients whose H-ECD level increases between 0 and 2 months, compared to patients whose H-ECD level decreases.

Pre-inclusion Screening Average Cost : € 829 per patient.

CONCLUSION

From an economic perspective, HER2 assays are cost effective : they are less expensive than cytotoxic and/or trastuzumab.

REFERENCES


CONTACT

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YEARS FOLLOW

(1,3)

€ 829 per patient

• Pre-inclusion Biochemical Methods
  - IHC (Immunno-Histochemistry) test determines the HER2 status.
  - When HER2 status is 2+, HER2/new amplification has to be evaluated by the FISH (Hybridisation In Situ par Fluorescence) method.
  - The H-ECD level is measured by ELISA (Enzyme Linked ImmunoSorbant Assay) technique.

• Statistical Methods
  - Survival Analysis : Overall Survival, Time to Tumour Progression, Time to Treatment Failure, Progression Free Survival (Kaplan-Meier Method, log-rank test)
  - Correlations : Relative risk, McNemar test, Kappa

• Economic Analysis :
  - Overall patient management cost includes pre-inclusion screening cost and treatment cost.
  - Treatment cost was calculated by adding DRG costs (2004) and onerous drug reimbursed over DRGs.
  - Drugs acquisition and biological and radiological examinations components were replaced by molecular real costs (prices AP-HP and CRLCC from 2001 to 2004) and by the costs of biological, cardiac and tumour volume assessments and IHC and FISH methods from NGAP 2004 (general nomenclature of the professional acts).