Purpose

The objective of this study was to assess the cost-effectiveness of a dihydropyrimidine dehydrogenase (DPD) deficiency screening test, combining 2 complementary assays, genotyping and phenotyping, before fluoropyrimidine administration.

Introduction

5-FU remains the back bone of most chemotherapy regimens in digestive cancers. Though, it can provoke severe, even lethal, toxic side effects. The frequency of treatment-related deaths with the standard protocols of 5-FU is between 0.3% and 1.2% and frequency of WHO grade III-IV toxicities is between 25% and 30%. Furthermore, these toxicities mobilize significant resources. DPD, the 5-FU key metabolic enzyme is submitted to a genetic polymorphism. Acute and early 5-FU toxicity is mostly due to DPD deficiency. We developed a screening test with the objective to assess DPD activity and detect metabolic deficiency. Our aim was to provide a pretherapeutic detection of 5-FU metabolic deficiency and to individually adapt 5-FU dosing (5-FU/ODPM, Tax + Protocol / ODPM, France). This test consists of a comprehensive approach coupling DPD genotyping and phenotyping (didiouracil/uracil : UH2/U). On the one hand, this screening helps to prevent severe toxicities and their related costs. On the other hand, by itself, it is an additional cost to the treatment.

Patients and medico-economic design

Retrospective data from a population of patients treated for colorectal cancer: 2 complementary assays, genotyping and phenotyping, before fluoropyrimidine administration.

Costs

<table>
<thead>
<tr>
<th>Screening strategy</th>
<th>Standard strategy</th>
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</thead>
<tbody>
<tr>
<td>Cost of screening test</td>
<td>€15</td>
</tr>
<tr>
<td>Cost of treatment</td>
<td>€x</td>
</tr>
<tr>
<td>Cost of toxicities 1N</td>
<td>€42e</td>
</tr>
<tr>
<td>Total</td>
<td>€195e</td>
</tr>
</tbody>
</table>

Effectiveness

- Cycle 1: 99.5% vs. 94.2%
- Cycle 2: 99.1% vs. 93.1%
- Cumulative prevalences: 98.6% vs. 87.3%

ICER

- Incremental Cost: -31€
- Incremental Effectiveness: -11.30%
- ICER: 270€/toxicity

Conclusions

Pre-treatment screening test (5-FU/ODPM, Tax + Protocol / ODPM) combining DPD genotyping and phenotyping reduced 5-FU-induced severe toxicities and prevented induced deaths. Its cost was lower than that of toxicity medical care that it prevented, even when not taking in account other related costs (death...). It should be recommended before 5-FU administration.