Economic Burden of Metastatic Colorectal Cancer Patients in Greece

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Colorectal cancer (CRC) is the third most frequent cancer in the world and the second in Europe, accounting for 10% and 12.9% of all new cancer cases in 2020.1 Its global prevalence is expected to rise rapidly to >3 million cases per year by 2040.2

**Introduction**

Colorectal cancer (CRC) is the third most frequent cancer in the world and the second in Europe, accounting for 10% and 12.9% of all new cancer cases in 2020.1 Its global prevalence is expected to rise rapidly to >3 million cases per year by 2040.2

**Objective**

The aim of this study was to map the treatment pathway in metastatic colorectal cancer (mCRC) in Greece and to investigate the healthcare resource use associated with the management of the disease.

**Methods**

- The methodology followed was based on a two-step approach. First, the local treatment pathways and associated resource use were identified emerging from a panel of experts via a three round Delphi approach. Secondly, the total cost for each pathway were estimated, by assigning unit costs to resource use items.

**Local treatment pathway and resource use**

- An expert panel of 5 medical oncologists of public and private sector with expertise in mCRC was convened, in order to map the current local treatment algorithm and associated healthcare resource use.

**The treatment phases studied were:** pre-progression; disease progression and treatment failure.

**Cost estimation for each pathway**

- Unit costs were retrieved from publicly available sources, Ministry of Health, Greek National Drug Pricing Committee and publications. The National Regulator of Healthcare Services (EKPY) (2018) Government Gazette 4898/B/1.10.2018

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**The micro-costing method was followed for the estimation of costs.** Only direct medical costs were considered, which consisted of oncology drug costs, costs of resource utilization associated with medical consultations, diagnostic tests, imaging and procedures. The total cost is presented on an annual basis.

**The weighted cost per patient per mutation line estimation was based on percentages of each pharmacological treatment reported by the expert panel in order to add the additional cost of resource utilization.**

- Similar disease management/resource consumption was considered for all mCRC patients independent of mutation.

To estimate pharmacological, the average price per mg was calculated based on the hospital prices per package minus 5% (EOPY & Hospital purchase price), for all packages marketed in Greece. Prices were taken from the latest Price Bulletin of February 2021.

- In order to take into account the dosage changes and patients’ compliance for the regimens, relative dosage (RD) was used in all treatment categories.

- The cost of relapses were also added in the annual cost estimation. 1 relapse for the 1st line, 1.25 relapse for 2nd line and 1.75 relapse at 3rd line.

- In Table 1 the cost of pharmaceuticals is presented at hospital prices without taking into consideration any potential discounts ie. rebates & claw back or negotiated prices between pharmaceutical companies and negotiation committee, as this information is confidential and not published.

<table>
<thead>
<tr>
<th>Table 1: Pharmaceutical cost</th>
<th>Hospital prices – €, Unit cost (€)</th>
<th>Cost per mg (€)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prodrug</td>
<td>147.31</td>
<td>0.47</td>
</tr>
<tr>
<td>Fluorouracil</td>
<td>11.2</td>
<td>0.03</td>
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<tr>
<td>Cetuximab</td>
<td>13.26</td>
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<td>Panitumumab</td>
<td>1.10</td>
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<tr>
<td>Bevacizumab</td>
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<td>Irinotecan</td>
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<td>Capcitabine</td>
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<td>0.40</td>
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<td>Nivolumab</td>
<td>106.60</td>
<td>0.02</td>
</tr>
<tr>
<td>Pembrolizumab</td>
<td>2,229.89</td>
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<tr>
<td>Biologics</td>
<td>1,046.92</td>
<td>0.33</td>
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<tr>
<td>Ramucil (Ramucil–Ipsiragen)</td>
<td>445.82</td>
<td>1.05</td>
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<tr>
<td>Mammalian C</td>
<td>15.91</td>
<td>0.84</td>
</tr>
</tbody>
</table>

**Results**

- The mean age of mCRC patient reported by the expert panel is 64.6 years, with a 1.79 (S.D. 0.23) body surface area (BSA) and 47.3% male.

- Among CRC patients, the 36.6% will become metastatic, from whom RAS mutation occurs in 45% of patients, BRAF mutation occurs in 8%, RAS/BRAF WT left occurs in 30% and RAS/BRAF WT right occurs in 17%, MSI-H DMMR occurs in 5% of patients despite local advanced disease.

- At Table 2 the pharmacological treatment options are presented at 1st, 2nd and 3rd line for all mutations.

**Resource utilization**

- The periods pre-and post-progression were reported on a monthly basis and were considered of similar disease management for all lines. Resource utilization data during stable disease, at progression, beyond third line and the respective cost are presented at Table 3.

Cost per line & Mutation

- In Figure 1 the monthly cost of mCRC patient per mutation and line is presented.

- The weighted annual cost of mCRC patient at 1st line was estimated at €277,340 at 2nd line €33,568 and at 3rd line €255,500.

- RAS/BRAF WT left had the highest cost at 1st line corresponding to 17% difference versus the average weighted cost, at 2nd line MSI-H DMMR cost was more than 2 times higher compared to the average 2nd line cost while at 3rd line BRAF Mutation cost was 74% higher than the average weighted cost.

Discussion

- Patients with metastatic CRC have 5-year survival rate less than 10% with poor quality of life.3,4 The present study investigated and provided an overall view of the resource use and associated costs required to treat metastatic CRC patients in Greece.

- According to our results, at 1st, 2nd and 3rd line treatment most patients receive biological targeted therapies in combination with chemotherapy (74.8%, 58.6% and 56% respectively) regardless of mutation.

- Although the current focus is on cost and efficacy of the disease, and mCRC seems to be a high-cost disease area, additional emphasis should be based on the survival benefits and improvements in patients’ quality of life that the new pharmaceutical advancements have brought into mCRC patients’ lives.