Economic Burden of Metastatic Colorectal Cancer Patients in Greece

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Introduction

Colorectal cancer (CRC) is the third most frequent cancer in the world and the second in Europe, accounting for 10% & 12.9% of new cancer cases in 2020.[1,3] 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 health care 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 costs for each pathway were estimated, by assigning unit costs to resource use items.

Local treatment pathway and resource use

- An expert panel of 6 medical oncologists of public and private sector with expertise in mCRC was convened, in order to map the current local treatment algorithm and associated health care resource use.
- The treatment phases studied were: pre-progression; disease progression and terminal care.

Cost estimation for each pathway

- Unit costs were retrieved from publicly available sources, Ministerial Gazette, DRG cost and other healthcare sources.[4] The perspective adopted was that of the Greek National Services Organization (EOPYY).
- 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, home care, hospital visits, laboratory tests, imaging examinations and procedures. The cost analysis is presented on monthly and annual basis.
- The weighted cost per patient per mutation per line estimation was based on percentages of each pharmacological treatment reported by the expert panel by adding the additional cost of resource utilization. Similar disease management/resource consumption was considered for all mCRC patients independent of mutation.
- To estimate pharmaceutical costs, the average price per mg was calculated based on the hospital prices per package minus 5% (EOPYY & 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 dose intensity (RDI) 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. Rebate & claw back or negotiated prices between pharmaceutical companies and negotiation committee, as this is information is confidential and not published

Table 1: Pharmaceutical cost

	Hospital prices – 5%, Unit cost (€)	Cost per mg (€)
Irinotecan	147.31	0.47
Folinic acid	11.2	0.03
Fluorouracil	14.14	0.0028
Cetuximab	132.26	1.32
Panitumumab	1,100.28	2.75
Bevacizumab	204.52	2.05
Aflibercept	250.27	2.50
Oxaliplatin	19.82	0.40
Capecitabine	10.66	0.002
Nivolumab	2,106.87	8.78
Pembrolizumab	2,229.89	22.30
Encorafenib	1,046.92	0.33
Tas102 (Trifluridine-tiporacil)	445.92	1.05
Regorafenib	1,884.71	0.56
Mitomycin-C	15.91	0.84

Results

- The mean age of mCRC patient reported by the expert panel is 64.6 years, with 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 patient in disease progression (2nd line).
- At table 2 the pharmaceutical 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 €27,340, at 2nd line €33,568 and at 3rd line €25,550.
- 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 (166%) compared to the average weighted cost while at 3rd line BRAF Mutation cost was 74% higher than the average weighted cost.

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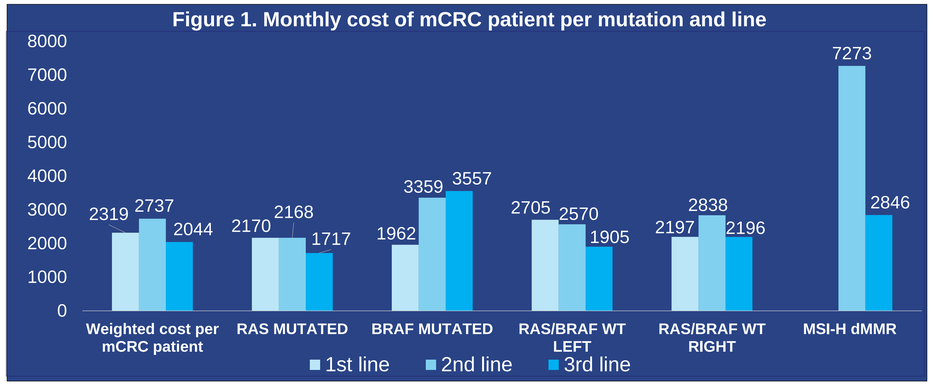
Table 2. Treatment options per mutation and line (% of patients)

	RAS MUTATED			BRAF MUTATED			RAS/BRAF WT LEFT			RAS/BRAF WT RIGHT			MSI-H dMMR	
	1st line	2nd line	3rd line	1st line	2nd line	3rd line	1st line	2nd line	3rd line	1st line	2nd line	3rd line	2nd line	3rd line
Folfiri	5	10	10	10	20				20	5				70
Folfiri & Cetuximab							15	5	10		15	10		
Folfiri & Panitumumab							20	5			25	10		
Folfiri & Bevacizumab	15	20		15	25		10	30		20	10			
Folfiri & Aflibercept		15			10			10			10			
Folfox	5	5	5	10							10			
Folfox & Cetuximab					10		15	5						
Folfox & Panitumumab							20	5						
Folfox & Bevacizumab	35	15		5			10	28		10	10			
Folfoxiri	3			20						20				
Folfoxiri & Panitumumab										5				
Folfoxiri & Bevacizumab	12			30						30				
Capecitabine			5											
Capecitabine & Oxaliplatin (CapOX)	3	10												
CapOX & Bevacizumab	12	10		10										
Capecitabine & Bevacizumab	10	10					10	10	10	10	10	10		
Tas102			50			40			40			40		
Regorafenib			30			10			10			10		
Encorafenib & Cetuximab					25	50								
Cetuximab									10			10		
Panitumumab												10		
Immunotherapies		5			10			2			10		100	30
TOTAL	100	100	100	100	100	100	100	100	100	100	100	100	100	100

Table 3: Resource utilization and cost during stable disease (pre/post progression), at progression and beyond third

	Pre-/post-progression period for 1st-2nd-3rd lines (times per month)*	Beyond 3rd line period (times per month)**	One-off resource use during progression 3-month period (times)***	Unit costs (€)
	Medical consultations			
Medical oncologist consultation	0.73	1.6	3	10.80
Radiation oncologist consultation	0.083			10.80
Oncology nurse visit	0.66	1.3	3	5.00
GP consultation	0.2	1	1	10.00
Psychology specialist consultation	0.08			15.00
Surgeon consultation	0.08			10.00
	Hospital visits			
Inpatient stay (oncology/general ward)	0.06		2	80.00
Emergency department visit	0.083			No cost
Day hospital visit	0.66	0.5	3	40.00
	Home care			
Best supportive care physician/nurse visit		2		7.30
Home aid (non-medical specialist)		2.3		5.00
	Examinations			
Whole-body CT	0.32		1	140.00
Brain MRI	0.033			236.95
Brain CT-scan	0.016			71.11
Chest radiograph	0.13			4.05
PET-CT scan	0.033			700
Bone scan	0.05			34.42
Blood test (CBC)	1		3.71	2.88
	Procedures			
Radiotherapy fraction	0.033			250.00
Surgical intervention	0.033			1,306.00

Figure 1. Monthly cost of mCRC patient per mutation and line



Discussion

- Patients with metastatic CRC have 5-year survival rate less than 10% with poor quality of life.[7-8]
- 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 analysis focuses on the cost of the disease, and mCRC seems to be a high-cost disease area, additional emphasis should be based on the survival benefits and improvement in patients' quality of life that the new pharmaceutical advancements have brought into mCRC patients' lives.

References

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