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Healthcare Resource Utilization (HCRU), effectiveness and safety of Trifluridine/Tipiracil in treatment of refractory metastatic colorectal cancer in a Portuguese Comprehensive Cancer Center (PCCC)

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BACKGROUND

- Worldwide, colorectal cancer represents 10% of all types of cancer, with 1.9 million new cases annually and 935,000 deaths, according to the Globocan survey (2020).
- Trifluridine/Tipiracil (FTD–TPI) is a drug approved for refractory metastatic colorectal cancer (mCRC) treatment [1].
- Clinical trials results showed positive efficacy and safety of FTD–TPI, but real-world evidence is needed [2].

OBJECTIVES

- To assessed HCRU and FTD–TPI clinical outcomes in a real-world (RW) setting.
- To describe demographic and clinical characteristics at baseline and follow-up and to evaluate health outcomes, such as treatment duration (TD), overall survival (OS), progression free survival (PFS), grade ≥3 adverse events (AE), as well as HCRU.
- To perform an exploratory post hoc analysis to analyze the cost per patient that are treated exclusively at IPO-Porto with FTD–TPI and have no multiple primary tumors.

METHODS

Study design

- Real-world retrospective cohort study.
- Lines of therapy (LOT) were defined based on disease progression, where a new line is determined to have started due to disease progression.

Population

- All mCRC patients who started FTD–TPI as palliative treatment before 01/11/2022.

Follow-up

- Patients were followed until 30/04/2023.

Outcomes

- PFS, OS, TD, grade ≥3 AE and HCRU.

Data collection

- Real-world data was collected from medical charts or Electronic Medical Record (EMR) and administrative records, including demographic and clinical data, type of treatment, treatment effectiveness and treatment costs.
- HCRU outcomes included: outpatient and emergency room visits; hospitalizations; complementary diagnostic and therapeutic procedures (CDTs).

Statistical analysis

- Patients' characteristics were summarized using descriptive statistics. Kaplan-Meier method was used for survival analysis.
- The micro-costing technique and the bottom-up approach were used. All medical direct costs (only hospital perspective), were accounted individually for each patient. The unit costs were obtained from National prices [3-4] or from the institution costs (Table 1). Cost data were aggregated on descriptive statistical tables and expressed as mean cost per patient.
- We followed a conservative approach in costing HCRU; costs were summarized related with all healthcare resources consumed during the treatment with FTD–TPI (between TAS-102 starting date and 30 days after the date of the last cycle).

Table 1. Unitary costs

Healthcare resource	Unitary cost	Source/Comment
Hospitalization	DRG depends of the episode	*Anexo III* [3]
Outpatient visits – specialist	€ 34.10 first visit € 31 follow-up visit € 25 without patient	Art. 15 [3]
Unplanned urgent visits – specialist	€ 31	Art. 15 [3]
Outpatient visits – other	€ 16	Art. 15 [3]
CDTs	Price dependes on the code of the exam	*Anexo IV* [3]
Radiotherapy, session	€ 104.53 € 250.92	Code 45182 and 45194, simple and complex radiotherapy
Drugs	Atual prices	

Abbreviations: DRG – Diagnosed Related Groups

RESULTS

- The cohort included 196 patients, 65% male, with a median age of 63/yo (23-85).
- Majority had an ECOG1 (62%) and 47% had ≥3 metastatic sites at treatment initiation.

Table 2. Patients demographics and clinical characteristics.

	N	%
Nr of Patients	196	100%
Median age (min-max)	63	(23-85)
Age group		
<65	124	63%
>=65	72	37%
Sex		
Male	127	65%
Female	69	35%
Primary site of disease		
Colon right	44	22%
Colon left	92	47%
Colon SOE	2	1%
Rectum	58	30%
KRAS mutation		
No	84	43%
Yes	110	56%
Missing	2	1%
NRAS mutation		
No	146	74%
Yes	9	5%
Missing	41	21%
BRAF mutation		
No	99	51%
Yes	11	6%
Missing	86	44%
Microsatellite instability (MSI)		
Yes	7	4%
No	164	84%
Not evaluated	25	13%
Carcinoembryonic antigen (CEA), ng/mL		
Median value at baseline	87,2	
≤5 ng/mL	10	5%
>5ng/mL	178	91%
missing	8	4%
Stage at diagnosis		
I	7	4%
II	14	7%
III	58	30%
IV	111	57%
missing	6	3%
Degree of differentiation		
Grade 1	15	8%
Grade 2	95	48%
Grade 3	10	5%
Indeterminated	76	39%
Time from diagnosis to 1st metastization		
<18 mo	152	78%
≥18 mo	44	22%
No. of metastisis		
1	28	14%
2	76	39%
>3	92	47%
Surgery primary tumor		
yes	162	83%
Surgery metastatic disease		
yes	90	46%
HIPEC		
yes	4	2%
Prior systemic anticancer agents		
Fluoropyrimidine	193	98%
Irinotecan	196	100%
Oxaliplatin	191	97%
Bevacizumab	159	81%
Anti-EGFR monoclonal antibody	88	45%
Encorafenib	1	1%
Imunotherapy	0	0%
ECOG performance status (Beginning of Treatment)		
0	67	34%
1	122	62%
2	7	4%

Table 3. Treatment characteristics.

	N	%
Median treatment duration - months	3,3	
Line of treatment Tas102		
2nd line	10	5%
3rd line	172	88%
more than 3 lines	14	7%
Best response to treatment		
CR	0	0%
PR	2	1%
ST	18	9%
DP	173	88%
missing	3	2%
Median of cycles (min-max)	3	(1-28)
Cycle postponement	108	55%
Dose reduction	47	24%

Health Care Resource Utilization

Table 4. Healthcare resources utilization

	sum	mean	median	minimun	maximum
Medical appointments	1641,0	9	7	1	53
Non-medical appointments	524,0	3	2	0	14
Emergency room	274,0	1	1	0	9
Bone scintigraphy	10,0	0	0	0	2
PET-CT	3,0	0	0	0	1
MRI	5,0	0	0	0	2
CT-scan	214,0	1	1	0	8
Clinical laboratory analysis	1307,0	7	6	0	45
Other exams	447,0	2	2	0	12
Radiotherapy sessions	32,0	5	5	0	10
Hospitalizations	99,0	1	0	0	7
Lenght of stay (days)	NA	4	0	0	54

i) Minimum 0 correspond to at least one patient who did not consume hospital resources in this activity category.
ii) CDTs performed during hospitalization are not considered in the counts. Its cost is valued in the value of the DRG

- There were a median of 7 medical appointments and 1 CT scans performed during treatment.
- Proportion of patients admitted in emergency was 54,4%; 29,2% were hospitalized.

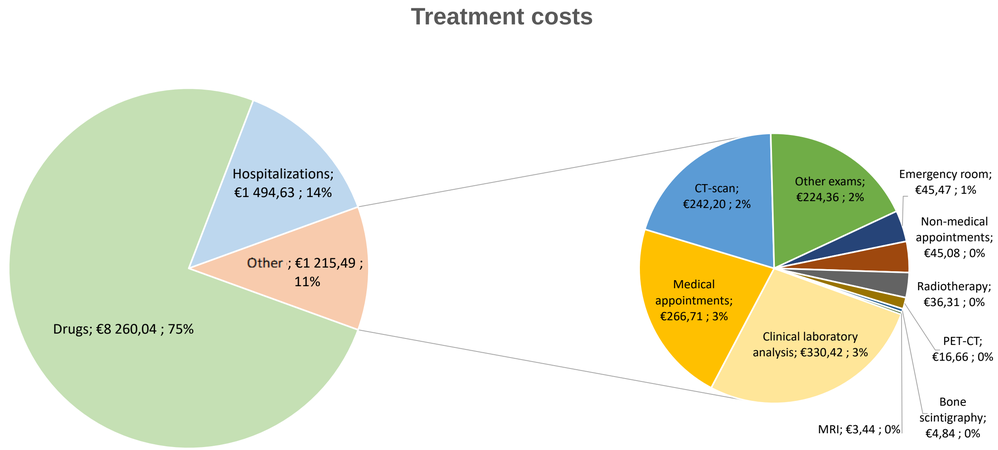

Figure 1. Treatment costs - average cost per patient; cost drivers

- The mean cost per patient was 10.639,73€.
- Drugs expenses accounted for 75% of the overall cost, followed by hospitalizations representing 14% of the cost.
- When drug acquisition cost was excluded, mean total cost was 2379,69€ per treated patient.

Safety

- Grade ≥3 adverse events(AE) occurred in 43% of the patients, the most common were neutropenia(31%) and anemia(8%).
- 4% patients hospitalized within 72 hours after toxicity.
- No toxic deaths were documented.
- AE led to dose reductions in 24% of the patients and treatment delays in 55%.

Effectiveness outcomes analysis

- Disease control rate was 10%.
- Median time to worsening of ECOG ≥2 was 5.3 months.
- Median PFS was 3.0 months and OS was 6.4 months (figures 1 and 2, respectively).
- In a subgroup analysis stratified by number of metastatic sites (2 vs 3 vs ≥3), median PFS was superior in patients with fewer sites involved (9.6 vs 6.8 vs 5.2 months).

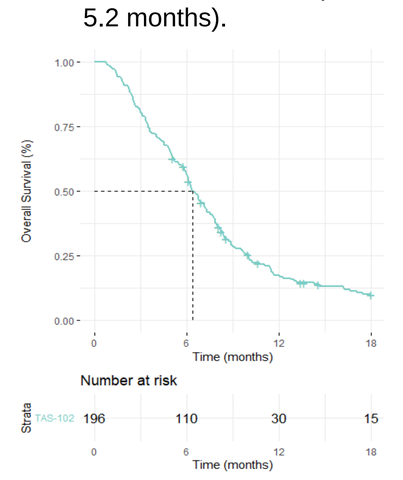

Figure 2. Overall survival

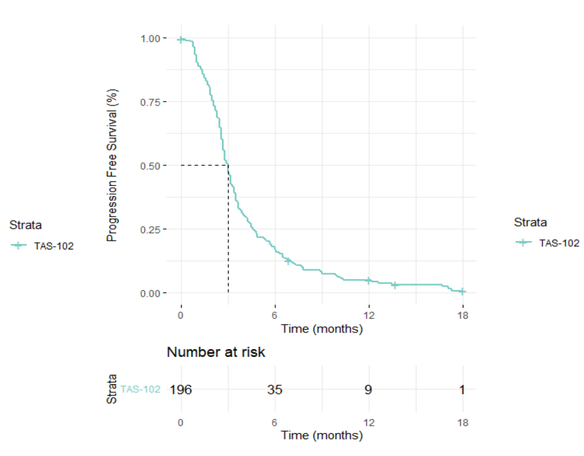

Figure 3. Progression free survival

CONCLUSIONS

- Given the high prevalence of mCRC patients, the treatment is likely to result in higher budget impact for hospitals.
- Our study showed more frequent dose reduction, worse disease control rate and a safety profile with fewer grade ≥ 3 AE reported compared to clinical trials.
- Survival benefits and time to worsening of performance status were comparable to the ones reported.
- Hospitalizations and exams may be underestimated because only costs carried out at the IPO-Porto were considered. There may be urgent admissions in the residence hospital, which we do not have information about, as well as patients bringing exams performed outside IPO Porto.

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