Medico-Economic Contribution of Screening for Dihydropyrimidine Dehydrogenase Deficiency in the Treatment of Colorectal Cancer With Fluoropyrimidines

Mansouri K[1], Attar FZ[1], Ramdani N[1], Oukkal M[2]
[1]University of Algiers 1, Algiers, Algeria, [2]CHU Issad Hassani, Algiers, Algeria

ABSTRACT

Introduction: Screening for dihydropyrimidine dehydrogenase (DPD) is an essential step in oncology, enabling the identification of patients at risk of severe toxicity to fluoropyrimidine-based drugs. This study aims to assess the medico-economic impact of DPD screening in colorectal cancer (CRC) patients in Algeria. **Methodology:** The method was based on the retrospective collection of patient data admitted to the oncology department between January 2021 and December 2023. The data concerned therapeutic management protocols, and the costs associated with this management according to two scenarios, one without systematic DPD screening and the other after the introduction of screening. A pharmacoeconomic model was used to estimate national expenditure on CRC management over a five-year time horizon . **Results and discussions:** The study included 403 CRC patients, 137 of whom suffered serious side effects from treatment, The cost of CRC management (without screening) was estimated at nearly was 1.46 million EUR(2023). This compares with 1.43 million EUR(with screening), with an avoided cost of more than 36.83 thousand EUR. On a national scale, the cost of treating patients amounted to more than 152.23 million EUR without screening (2028), compared with 147.81 million EUR with screening (2028), taking into account the 9.37% rate of deficiency. The cost avoided is estimated at more than 3.96 million EUR(2028). Assuming a deficit rate of 15%, screening would save more than 8.14 million EUR(2028). These savings can be explained by the reduction in serious side-effects and the improvement in patients' quality of life. **Conclusion:** DPD screening prior to chemotherapy treatment for colorectal cancer is proving cost-effective in Algeria. It reduces the cost of serious side effects and improves patient care.

INTRODUCTION

Pharmacoeconomics is now vital in oncology, providing essential insights for stakeholders across the pharmaceutical industry, healthcare, and public health (1). CRC is one of the most prevalent malignant tumors, with severe consequences (2). Fluoropyrimidines, particularly 5-fluorouracil (5FU) and its oral prodrug capecitabine, are the most prescribed treatments (3). However, these medications can cause severe toxicity in 10 to 40% of patients, with fatal outcomes in 0.2 to 0.8% (4). Toxicity may be linked to a deficiency in the enzyme DPD, which is crucial for metabolizing 5FU, Complete DPD deficiencies are rare (0.1% to 0.5%), while partial deficiencies are found in (3% to 15%) of patients (5). Screening for DPD can be performed through genotyping or phenotyping, but there's no established consensus on on screening methods (6). Screening for DPD deficiency is recommended before treatment initiation to prevent toxicity and improve clinical outcomes (7).
Notably, there are no established guidelines in Algeria for systematic DPD screening in patients with this type of cancer.

OBJECTIVE :

Our study aims to estimate the contribution of DPD screening in managing colorectal cancer with fluoropyrimidines, particularly to reduce costs associated with treatment-related side effects. Currently, there are no systematic screening recommendations for DPD in Algeria for patients with this type of cancer. This pharmacoeconomic analysis compares the costs incurred in treating patients who did not undergo DPD screening to those who did.

METHODS

This study aimed to assess the medical and economic benefits of screening for DPD in the management of CRC by comparing treatment costs with and without DPD screening.

A retrospective analysis was conducted on adult patients treated at CHU Beni Messous from January 2021 to December 2023. Data were collected on patient demographics, medical history, clinical signs, examination data, treatment protocols, and adverse effects.

Data collection and subsequent analysis were conducted using an Excel model.

Cost estimations for managing CRC were derived from various components: diagnostic and extension examinations, follow-up tests, and treatments.

Prices for diagnostic tests were obtained from private clinics and medical laboratories, while treatment costs for adjuvant and neoadjuvant therapies were sourced from the central pharmacy at CHU Beni Messous (excluding targeted therapies). Costs associated with managing adverse effects were gathered from the central pharmacy and private pharmacies, focusing solely on those induced by fluoropyrimidines.

The total cost for CRC management was calculated using the formula:

Total Cost = Σ[((cost of diagnostic tests) + (treatment cost) + (adverse effect management cost)) × number of patients]

The pharmacoeconomic evaluation compared two scenarios:

First scenario: management of CRC without DPD screening.
Second scenario: management of CRC with DPD screening.

This involved estimating the weighted average cost per patient and the total cost for the studied population without screening, followed by a similar analysis for those with systematic DPD screening, including specific costs for patients with DPD deficiency.

Data collection were extrapolated to a national scale using an economic model, the study identified the eligible population and estimated costs for both scenarios in 2023, considering deficiency rates of 9.37% and 15%, with a simulation of their evolution over 5 years, considering only demographic and prevalence rates changes and assuming constant expenses .

RESULTS

A total of 403 patient records were studied to assess the economic impact of treatment-related adverse effects in colorectal cancer (CRC). Of these, 137 patients experienced severe adverse effects, while 266 had mild effects or no complications.

First scenario: Costs Without DPD Screening
The average cost per patient was 3,521.75 EUR, rising to 4,737.48 EUR for undiagnosed deficient patients.
The total cost for managing CRC in this group was 1.46 million EUR.

Second scenario: Costs With Systematic DPD Screening
Among the patients, 64 were screened for dihydropyrimidine dehydrogenase (DPD), identifying 6 with partial deficiencies. It is estimated that 37 patients have a DPD deficiency (9.37%). The management cost for a deficient patient was 3,043.88 EUR.
The costs for undiagnosed deficient patients accounted for nearly 175,508.77 EUR.
The total cost for managing CRC with systematic DPD screening was 1.43 million EUR.

Pharmacoeconomic Modeling
The costs obtained pertain to the population affected by colorectal cancer (CRC) in Algeria. In 2023, the national prevalence is estimated at 23,047 patients (8.9), based on the national population for the same year (10). According to GLOBOCAN estimates (11), the incidence of CRC is evolving, as shown in Figure (2).
The costs associated with managing CRC for the eligible population over a five-year horizon from 2023 to 2028, considering that 9.37% of the population is DPD deficient, are presented in table (1). Similarly, the costs associated with managing CRC for the eligible population, considering that 15% of the population is DPD deficient, are presented in the table(2).

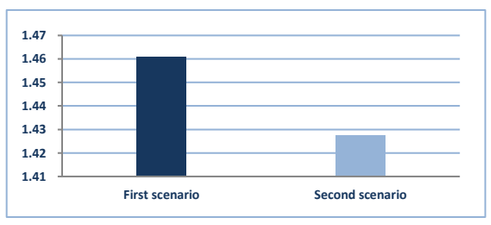

Fig.1 : Total costs for managing CRC without and with DPD screening for the studied patients N=403 from 2021 to 2023 in MILLION of EUROS

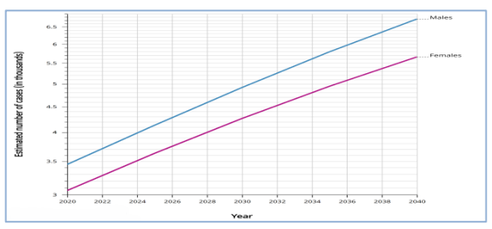

Fig.2 : Estimated Number of New Colorectal Cancer Cases from 2020 to 2040 by Gender (Ages 20-85) in Algeria

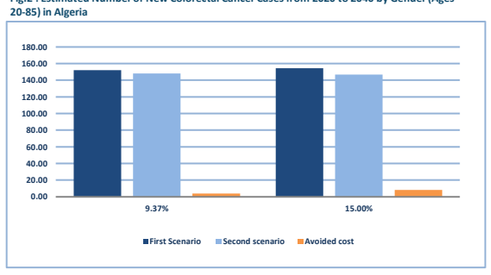

Fig.3 : Estimated annual costs for managing CRC in 2028 with and without DPD screening in Algeria in MILLION of EUROS

Tab.1 : Cost Evaluation Over a 5-Year Horizon with 9,37% Deficiency

Year	Eligible Population	Cost without Screening (EUR) in millions	Cost with Screening (EUR) in millions	Avoided Cost (EUR) in millions
2023	23047	83.37	81.55	2.19
2024	26538	96.23	93.91	2.51
2025	30123	109.55	106.49	2.85
2026	33894	123.11	119.64	3.22
2027	37804	137.15	133.38	3.58
2028	41808	152.23	147.81	3.96

Tab.2 : Cost Evaluation Over a 5-Year Horizon with 15% Deficiency

Year	Eligible Population	Cost without Screening (EUR) in millions	Cost with Screening (EUR) in millions	Avoided Cost (EUR) in millions
2023	23047	85.37	80.88	4.49
2024	26538	98.23	93.17	5.16
2025	30123	111.99	105.57	5.86
2026	33894	125.77	119.68	6.59
2027	37804	140.04	132.93	7.35
2028	41808	154.86	146.75	8.14

DISCUSSION

Our study involved 403 colorectal cancer patients, with 137 experiencing grade 3 to 4 adverse effects. Among 64 screened patients, 6 were DPD deficient. In 2023, the estimated cost of managing these patients without screening was approximately 1.46 million EUR, with a weighted average cost of 3,521.75 EUR per non-deficient patient and 4,737.48 EUR per undiagnosed deficient patient. The costs for undiagnosed deficient patients accounted for nearly 175,508.77 EUR, or 9.37% of the population. With systematic screening, the total management cost dropped to around 1.43 million EUR.

For the eligible population in Algeria, the costs without screening were over 152.23 million EUR, compared to 147.81 million EUR with screening (assuming a 9.37% deficiency rate), yielding an avoided cost of 3.96 million EUR (2.68% of the expenditure without screening). With a 15% deficiency rate, the total cost without screening increased to over 154,86 million EUR, versus 146.75 million EUR with screening, resulting in savings of over 8.14 million EUR. Our findings emphasize the financial benefits of DPD screening in managing adverse effects.

CONCLUSION

The cost of managing colorectal cancer (CRC) with fluoropyrimidines in Algeria represents a significant economic burden, which continues to rise annually due to adverse effects in non-screened patients. DPD screening is essential for determining DPD status; it helps reduce adverse effects associated with this deficiency and mitigates the related costs.

REFERENCES :

1. Introduction à la pharmaco-économie bibliothèque du nouveau monde les presses de l'université de montréal Auteurs Anne Crochard-Lacour, Jacques LeLorier, Introduction à la pharmacoéconomie - Anne Crochard-Lacour, Jacques LeLorier - Google Livres
2. Institut national français du cancer Définition cancer (e-cancer.fr)Définition cancer (e-cancer.fr)
3. world health organization Cancer colorectal (who.int) 11 juillet 2023 Cancer colorectal (who.int)
4. Mis en ligne le 30 avril. 2019 Haute Autorité de Santé - Cancer : recherche d'un déficit en enzyme dihydropyrimidine déshydrogénase (DPD) avant chimiothérapie (has-sante.fr)
5. Le groupe cerba healthcare . Dépistage du 5-FU (DPD) par phénotypage et génotypage (lab-cerba.com)
6. Loriot MA et al. Dépistage du déficit en dihydropyrimidine déshydrogénase (DPD) et sécurisation des chimiothérapies à base de fluoropyrimidines : mise au point et recommandations nationales du GPCO Unicancer et du RNPGx. Bull Cancer avril 2018; 105: 397–407.
7. American society for clinical pharmacology and therapeutics . Pourquoi y a-t-il encore un débat sur la recommandation du test DPYD avant le à la fluoropyrimidine https://ascpt.onlinelibrary.wiley.com/doi/full/10.1002/cpt.3016
8. Annuaire statistique de la wilaya d'alger 2020 https://alger.mta.gov.dz/wp content/uploads/sites/6/2022/03/ANNUAIRE-STATISTIQUE-DE-LA-WILAYA-D'ALGER-2020.pdf
9. Le registre des tumeurs d'Alger de 2020. https://www.insp.dz/images/PDF/Les%20registres/TumeursAlger/Registre_Alger_2020.pdf
10. Office National des statistiques. ONS : Office National des Statistiques
11. Global Cancer Observatory. https://gco.iarc.who.int/tomorrow/en/dataviz/trends?multiple_populations=1&cancers=41&populations=12&group _populations=1&types=0&age_start=6

Contact for further information: **Pr. Kamel Mansouri**, Faculty of pharmacy university of algiers 1; **Mansourikamel369@gmail.com**
Dr. Fatma Zohra Attar : **Fatmazohraattar@outlook.com** , **Dr. Nihad Ramdani** : **Nihad.ramdani1998@outlook.com**