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ORIGINAL RESEARCH

Tinzaparin for the Management of Cancer Associated Thrombosis in Patients with Cancer: a Budget Impact Analysis from the Italian Healthcare System Perspective

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ABSTRACT

BACKGROUND: Venous thromboembolism (VTE), which includes deep vein thrombosis (DVT) and pulmonary embolism (PE), is a significant health problem with especially increased prevalence, morbidity and mortality in patients with cancer. This study aimed at assessing the economic impact of tinzaparin in patients with cancer associated thrombosis (CAT).

METHODS: A budget impact model (BIM) was developed to assess the economic impact of tinzaparin as treatment for patients with CAT. The analysis was conducted over a 3-year time horizon and by adopting the Italian Healthcare system perspective. The model estimated and compared direct medical costs associated with tinzaparin (scenario with tinzaparin) to the ones associated without tinzaparin (scenario where only enoxaparin is available). Epidemiological data as well as VTE events' rates were retrieved from literature, while costs data were retrieved from the Italian rate tables. The model estimated the economic impact as well as the economic variation associated with drug wastage and VTE management.

RESULTS: The model estimated 2,090, 4,202 and 5,429 patients potentially eligible to the treatment during the first, second and third year, respectively. The use of tinzaparin resulted in a cost saving of about €3 millions over 3 years (−€446,378 during the first, −€1,025,848 during the second, and −€1,657,508 during the third year). In the same timeframe, the use of tinzaparin also resulted in decreased costs associated with drug wastage (−€738,604) and recurrent VTE management (−€404,470).

CONCLUSIONS: Tinzaparin for the management of CAT patients has the potential for substantial savings, compared to treatments currently available. Stakeholders may consider these data to improve healthcare resource allocation in the Italian setting

Keywords

Thrombosis; Cancer; Low molecular weight heparin; Tinzaparin; Budget impact analysis

INTRODUCTION

Thrombosis represents one of the most serious and frequent complications in cancer patients, negatively impacting both prognosis and quality of life. In particular, cancer-associated thrombosis (CAT) is a complex condition that occurs when the tumor interacts with the hemostatic and vascular system, increasing the risk of thrombotic events (venous thromboembolism, VTE) such as deep vein thrombosis (DVT) and pulmonary embolism (PE) [1,2]. This pathological interaction further complicates the clinical management of neoplastic disease, adding a level of complexity for both patients and clinicians.

The socioeconomic impact of CAT is multifactorial and significant. In addition to increased morbidity and mortality, thrombosis contributes to higher healthcare resource utilization, with prolonged hospitalizations and long-term antithrombotic therapies [3]. This leads not only to a deterioration in the quality of life for patients and their caregivers but also to an increased workload for national healthcare systems, which must manage a more complex and demanding caseload [4,5]. Moreover, thrombosis can negatively influence the effectiveness of anticancer therapies, reducing the likelihood of treatment success and compromising the overall prognosis of cancer patients. This implies not only greater complexity in the clinical management of the disease but also an increase in the costs associated with anticancer treatments

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and the management of thrombotic complications. Management of VTE relies on anticoagulation therapy, which may last up to 6 months to avoid recurrence due to the high risk during the first months after primary VTE [6]. The latest guidelines from the American Society of Hematology (ASH), the International Society on Thrombosis and Haemostasis (ISTH), the National Comprehensive Cancer Network (NCCN), the Initiative on Thrombosis and Cancer (ITAC), and the American Society of Clinical Oncology (ASCO) recommend the use of low molecular weight heparin (LMWH) or a direct oral anticoagulant (DOAC) (apixaban or rivaroxaban) as anticoagulation therapy for the management of VTE in oncology patients [7–10]. LMWHs, such as tinzaparin, enoxaparin and dalteparin, are preferred for VTE management in cancer patients due to their efficacy and safety profile, without significantly increasing the risk of major bleeding. To date, the only approved drugs for the prolonged management of VTE in cancer patients in Italy are tinzaparin and enoxaparin.

Studies on the cost effectiveness and budget impact of treating CAT were carried out in several countries with contrasting results, some showing additional costs and some showing costs savings [11–15]. To the best of our knowledge, data on the economic impact associated with the use of tinzaparin are scarce. Therefore, this study aims at assessing the economic burden associated with the use of tinzaparin for the management of CAT prolonged treatment in the Italian setting.

MATERIAL AND METHODS

Model overview

An analytical budget impact model specifically adapted to the Italian healthcare context was developed in MS Excel. The model structure was designed to estimate over a period of 3 years the impact of tinzaparin introduction in the hospital setting for the management of patients with CAT. The model is based on epidemiological data concerning patients with CAT and VTE in Italy [16–18]. Economic data input for the model included the drug costs and those related to recurrent VTE management [19]. Specifically, the model firstly estimated the cost per patients within each treatment regimen, and this cost was then applied to the total number of patients treated, according with their weight, with each therapeutic alternative included in the simulation, based on the entered market share. The model compared two scenarios: the scenario without tinzaparin, corresponding to current clinical practice (scenario without tinzaparin), versus the counterfactual scenario in which tinzaparin is available in the country.

The analysis was conducted in compliance with the methodological guidelines published by the International Society for Pharmacoeconomics and Outcomes Research (ISPOR) [20].

Study population

A structured literature review was carried out to identify sources of published data to populate the budget impact model with epidemiological data specific to Italy. The population being analyzed is represented by subjects with a cancer diagnosis and who experienced VTE events that can be managed with tinzaparin (Table I). At the time of the analysis, the available data estimated that there were 373,300 new cancer diagnoses in Italy in year one, with an annual growth rate of 0.5%. [21]. Therefore, patients with a diagnosis of cancer were 373,300 in the first year of the simulation, 375,167 in the second and 377,042 in the last year. Among patients with cancer, 8.00% had VTE, therefore the number of patients with cancer and VTE

Target Population	Year 1	Year 2	Year 3	Reference
Incident cancer patients in Italy (n)	373,300	375,167	377,042	AIOM 2018 [21], growth rate 0,5%
CAT patients with VTE				
• %	8.00	8.00	8.00	Ageno 2019 [17]
• n	29,864	30,013	30,163	Model estimation
CAT patients with VTE treated with enoxaparin				
• %	7.00	14.00	18.00	Cohen 2017 [6]
• n	2,090	4,202	5,429	Model estimation

Table I. *Number of patients eligible to the treatment during the study period*
CAT: cancer-associated thrombosis VTE: venous thromboembolism

Treatment	Year 1		Year 2		Year 3	
Patient	**%**	**n**	**%**	**n**	**%**	**n**
Scenario without Tinzaparin						
Enoxaparin	100	2,090	100	4,202	100	5,429
Tinzaparin	0	0	0	0	0	0
Scenario with Tinzaparin						
Enoxaparin	30	627	20	840	0	0
Tinzaparin	70	1,463	80	3,361	100	5,429

Table II. *Market share*

estimated in the model ranged from 29,864 during the first year to 30,163 during the third year [17]. Finally, as reported by Cohen and colleagues 7.00%, 14.00% and 18.00% of patients were treated with LMWH during the first, second and third year of simulation, respectively [6]. Consequently, the target population figures were determined to be 2090 patients in the first year, 4,202 in the second year, and 5429 in the third year (Table I).

Treatment data

In the model, tinzaparin was compared with enoxaparin, which has the indication for the prolonged treatment and recurrence prevention of VTE in patients with active cancer. The recommended duration of the prolonged treatment is 6 months as per Summary of product characteristics (SmPC).

Market share

In the scenario without tinzaparin the model assumed that all patients were treated with enoxaparin, therefore 2,090, 4,202 and 5,429 patients were assumed treated with enoxaprin during the first, second and third year, respectively. On the contrary, in the scenario with tinzaparin, the model assumed that 70% of patients were treated with tinzaparin during the first year. In this last scenario, the percentage of patients treated with tinzaparin were assumed to increase during the second and third year, with 80% and 100% of patients treated with tinzaparin, respectively. Therefore, in the new scenario, the number of patients treated with tinzaparin were 1,463 during the first year, 3,361 during the second year and 5,429 during the third year (Table II).

Clinical events

The clinical events considered in the model included recurrent VTE. Specifically, data from the literature showed a risk of VTE recurrence of 9,15% among patients treated with enoxaparin and of 6,23% among patients treated with tinzaparin [16,22–27].

Costs

The analysis was conducted considering the Italian NHS perspective, therefore only direct health costs were considered. Specifically, the costs associated with treatments and VTE management were considered. The drug acquisition costs for each therapy were computed as an annual expense by considering the unit costs and the daily dosage used by patients. For both treatments, the daily dosage varied in accordance with the weight of the patient as indicated by the European public assessment report (EPAR) provided by the European Medicine Agency and by SmPC as documented on the Italian medicine agency (AIFA) website. The weight distribution used in the base case was 3,82% patients in the range 43-48 Kg; 4,85% patients in the range 49-54 Kg; 6,52% patients in the range 55-59 Kg; 10,81% patients in the range 60-65 Kg; 14,85% patients in the range 66-71 Kg; 16,04% patients in the range 72-77 Kg; 12,48% patients in the range 78-82 Kg; 12,15% patients in the range 83-88 Kg; 8,62% patients in the range 83-94 Kg; 4,58% patients in the range 95-99 Kg; 5,28% patients in the range >100 Kg [22]. The ex-factory price for package, net of statutory discount (-5%, followed by -5%) was considered, in compliance with legal requirement for each reimbursed drug. Table III reported the different products containing enoxaparin and tinzaparin available in Italy and the dosage used in patients according with their weight [23]. The use of these therapies might produce waste of drug due to unused drug after dose administration. Therefore, the model includes also the cost of wastage associated with the adjustment of the daily dosage. Finally, the model includes the cost of VTE recurrence management (€1,349.00) [19].

Analyses

The model estimated the overall costs in the two scenarios compared for each of the 3 years simulated and for the whole period, and the differences associated to the scenario with tinzaparin as compared to the scenario without tinzaparin. The costs were also estimated and compared for each cost categories: costs of correct dosage (the cost associated to the percentage of patients that received the correct treatment dosage without wastage), costs of over dosage (the cost associated to the percentage of patients that received a treatment dosage associated to wastage), costs of wastage (the cost related to the drug wastage within the Costs of over dosage patients) and costs of VTE management.

Finally, to test the reliability of the results, a probabilistic sensitivity analysis was performed to test the effect of weights distribution on the overall 3 years budget impact estimated by the model. The analysis was performed assuming a Dirichlet distribution for the weights and performing 1000 simulations to draw a curve with all possible budget impact results.

Packaging (n syringe)	Dosage (IU)	Ex-factory Price (€/syringe)
Enoxaparin		
10	6,000	2.76
10	8,000	3.68
10	10,000	4.60
Tinzaparin		
10	8,000	3.54
10	10,000	4.42
10	12,000	5.31
10	14,000	6.19
10	16,000	7.08
10	18,000	7.96

Dose according with body weight				
Weight classes (Kg)	Tinzaparin		Enoxaparin	
	Dosage (IU)	Syringe use (€)	Dosage (IU)	Syringe use (€)
43–48	8,000	8,000	9,100	10,000
49–54	9,000	10,000	10,300	2x 6,000 12,000
55–59	10,000	10,000	11,400	2x 6,000 12,000
60–65	11,000	12,000	12,500	2x 8,000 16,000
66–71	12,000	12,000	13,700	2x 8,000 16,000
72–77	13,000	14,000	14,900	2x 8,000 16,000
78–82	14,000	14,000	16,000	2x 8,000 16,000
83–88	15,000	16,000	17,100	10,000 + 8,000 18,000
89–94	16,000	16,000	18,300	2x 10,000 20,000
95–99	17,000	18,000	19,400	2x 10,000 20,000
> 100	18,000	18,000	20,500	2x 10,000 20,000

Healthcare service	Annual cost (€)
Annual cost for VTE management	1,249

Table III. *Treatment and VTE recurrence management costs*

	Year 1	Year 2	Year 3	Overall
Scenario without tinzaparin (€)				
Overall	3,078,412	6,187,756	7,996,507	17,262,675
Costs of correct dosage	345,550	694,573	897,604	1,937,727
Costs of overdosage	2,474,886	4,974,639	6,428,782	13,878,307
• Costs of wastage	231,139	464,600	600,407	1,296,146
Costs management VTE	257,976	518,544	670,120	1,446,641
Scenario with tinzaparin (€)				
Overall	2,632,034	5,161,908	6,338,999	14,132,941
Costs of correct dosage	897,655	1,962,770	2,945,899	5,806,324
Costs of overdosage	1,534,103	2,813,175	2,937,169	7,284,446
• Costs of wastage	125,754	222,484	209,304	557,542
Costs management VTE	200,277	385,963	455,930	1,042,170
Change between the scenario with tinzaparin and the scenario without tinzaparin (€)				
Overall	-446,378	-1,025,848	-1,657,508	-3,129,734
Costs of correct dosage	552,105	1,268,197	2,048,295	3,868,598
Costs of overdosage	-940,783	-2,161,464	-3,491,613	-6,593,861
• Costs of wastage	-105,385	-242,116	-391,104	-738,604
Costs management VTE	-57,699	-132,581	-214,190	-404,470

Table IV. *Budget impact results scenario with tinzaparin (scenario with tinzaparin) versus scenario without tinzaparin (scenario without tinzaparin)*

RESULTS

The use of tinzaparin yielded an overall budget reduction exceeding €3 million over 3 years, corresponding to a percentage decrease of 18% compared to the budget in the scenario without tinzaparin. The availability of tinzaparin resulted in a cost saving of €446,378, €1,025,848, and €1,657,508 during the first, second and third year of simulation, respectively (Table IV). Furthermore, the availability of tinzaparin also resulted in a reduction of drug wastage costs and VTE management costs. Specifically, the use of tinzaparin resulted in lower number of patients with recurrent VTE and consequently in a reduction of associated costs: -€57,699 during the first year, -€132,581 in the second years and -€214,190 in the third year. Similarly, the use of tinzaparin resulted in a reduction of drug wastage cost of -€105.385, -€242.116 and -€391.104 in the first, second and third year, respectively.

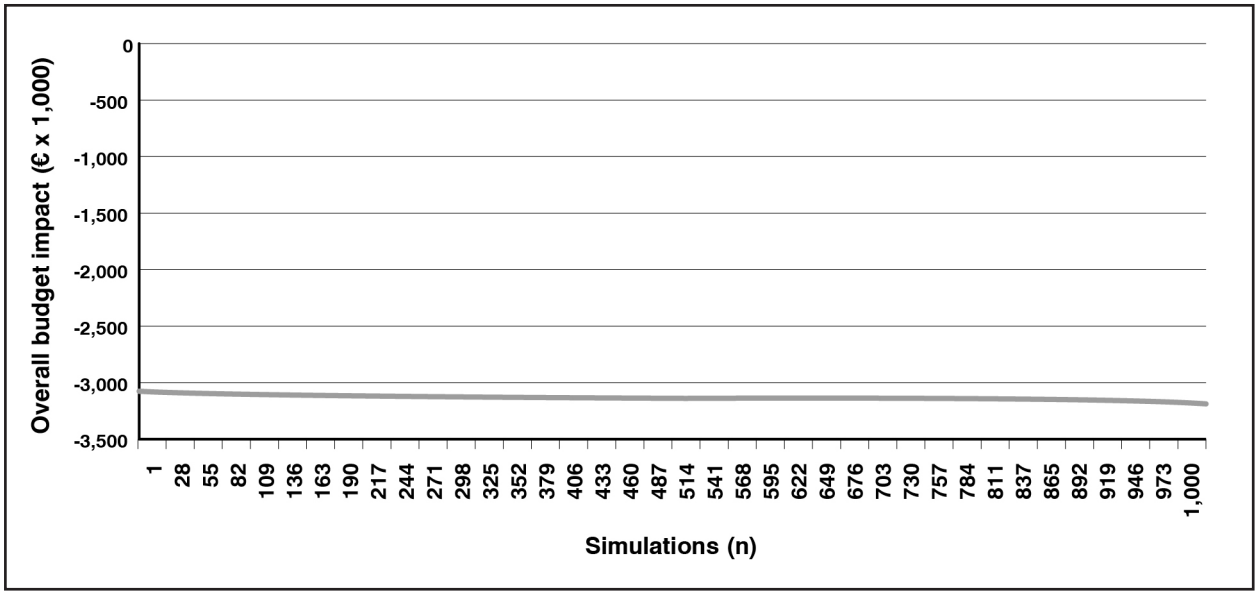

Figure 1. *Probabilistic sensitivity analysis: 3 years budget impact associated to tinzaparin*

The changes between the scenario without tinzaparin and the scenario with tinzaparin were calculated for each parameter (overall, costs of correct dosage, costs of wastage, and costs of management) by subtracting the cost associated to the scenario with tinzaparin to the scenario without tinzaparin. The correct dosage is the cost associated to the percentage of patients that received the correct treatment dosage without wastage; the costs of over dosage are the costs associated to the percentage of patients that received a treatment dosage associated to wastage; costs of wastage are the costs related to the drug wastage within the costs of over dosage patients.

The probabilistic analysis conducted to test the effects of body weights distribution on budget impact results are reported in Figure 1. The Figure shows how the 3-year budget impact associated to tinzaparin range from a minimum saving of €3,071,552 to a maximum of €3,177,172 over the 1000 simulations conducted.

DISCUSSION

This study attempted to analyze the affordability of tinzaparin compared to enoxaparin adopting the perspective of the Italian NHS. To our knowledge, it is the first study that aimed at assessing the economic burden of this drug when used as therapeutic option for the management of patients with cancer and VTE. Findings of the study reveal that the use of tinzaparin is associated with cost saving for the Italian NHS. Specifically, the use of tinzaparin is associated with a cost saving of over €400,000 during the first year and over €1,5 million during the third year. This is crucial considering that guidelines recommend prolonged treatment with low molecular weight heparins (LMWHs) in patients with cancer and VTE of the duration of 3 to 6 months, depending on cancer type and patients' characteristics [7–10].

Furthermore, treatment alternatives associated with reduced risk of VTE recurrence compared with the available therapeutic option is important considering the increased risk of mortality associated with CAT [5,24–26]. Our study showed that the use of tinzaparin was associated with decreased occurrence of VTE over the observational period, compared with enoxaparin. This data corroborates the positive impact of tinzaparin compared with the alternative.

From an economic standpoint, management of CAT represents a significant economic burden for patients and for the healthcare system [5,10]. In fact, the management of patients with CAT and VTE results in an increase of direct and indirect costs. Specifically, direct costs include expenses for antithrombotic therapies, diagnostic tests, and therapeutic procedures necessary to manage thrombosis. Indirect costs are equally relevant and encompass costs associated with hospitalizations, outpatient visits, and loss of productivity due to illness [27,28]. Our findings suggest that the use of tinzaparin compared with enoxaparin contributes to the reduction in the economic burden associated with VTE management.

In this context, it is important also to evaluate the wastage associated with the use of LMWHs. Our study showed that tinzaparin was associated to a reduction of wasted product compared with enoxaparin. This is important from both an environmental and an economic point of view. Considering the environmental impact, it is important for policy makers and society to take into account the environmental impact of a technology. For these reasons, several authors encourage, when possible, the use of eco-friendly technologies [29–31]. Considering the healthcare perspective, the use of a product such as tinzaparin, that results in a reduction of drug wastage and consequently in cost saving for the healthcare system might be preferable compared with a product with higher wastage and consequently higher environmental, health, and cost impact.

To the best of our knowledge, data on healthcare resource utilization and costs associated with the use of tinzaparin and other LMWH in patients with cancer is still scarce. However, recent studies highlighted that the occurrence of CAT and VTE, in patients with cancer is associated with increased cost of disease management (up to 50% higher), the majority of which were represented by direct costs [27,28,32]. This emphasizes the importance of prevention and management of VTE in patients with cancer and highlighted the necessity to focus on therapies that may contribute to decrease the healthcare economic burden. Thus, the findings of this study support the hypothesis that the introduction of tinzaparin into the Italian market will probably results in costs saving for the NHS in the management of patients with CAT, as compared to the currently approved available treatments.

Finally, the administration schedule of the two treatments might have an impact on the economic burden. In fact, it is possible to speculate that a drug administered once daily, such as tinzaparin, compared with a drug administered twice daily, such as enoxaparin, might result in improved efficiency in patient management, with a consequent reduction in general costs and, in particular, those associated with the waste and the risk of recurrence of the VTE event [27].

Our results corroborate also existing pharmaco-economic evaluation, which suggested that the use of tinzaparin compared with other therapeutic options resulted in cost saving for the health care system. However, it should be noted that previous researches investigated the economic burden of tinzaparin as treatment for thromboembolic diseases not associated with cancer [33]. Our analysis adds new data on the economic impact of this therapy in the context of VTE management in patients with cancer.

The incorporation of BIM into the decision-making framework represents a paradigm shift in healthcare management, facilitating a transition towards evidence-based resource allocation and value-oriented care delivery [34]. By providing a systematic framework for assessing the economic implications of healthcare interventions, BIM empower stakeholders to make informed decisions that optimize patient outcomes, enhance healthcare system performance, and ensure the prudent stewardship of financial resources. As healthcare systems continue to grapple with the challenges posed by CAT and other complex medical conditions, BIMs will play a crucial role in shaping the future of healthcare delivery, driving innovation, and promoting sustainability in the pursuit of better health for all. The possible economic consequences of the use of tinzaparin presented in this study represent a first estimate that will require further refinement, in light of the data on real use in the Italian treatment context.

This study has strengths and limitations. The main strength is that it is the first budget impact analysis of tinzaparin compared with another LMWH as treatment option for patients with cancer and VTE. Additionally, the study estimates the direct medical costs associated with VTE management and drug wastage, that is crucial from an environmental and clinical point of view. However, as with all modelling analyses, this analysis has limitations that should be considered when interpreting the results. First, the BIM relied on projected utilization rate of tinzaparin, as indicated in the market share data, which signifies that the findings may not be generalizable to populations with different adoption rates of the drug. Second, the analysis was based on wholesale acquisition costs (WAC) for drug acquisition, without accounting for undisclosed discount, which are not publicly available and can vary substantially across different countries. In this regard, in the analysis we used the ex-factory price, following the recommendation by AIFA guideline for the economic evaluation [35]. It should be noted, however, that drug price may be subject to confidential discounts negotiated at national level between AIFA and the pharmaceutical company, which are applicable to any regional or local procurement. This could lead to lower actual prices due to undisclosed discounts or competitive tenders for both enoxaparin and tinzaparin. Finally, the epidemiological data used for the analysis have been recently updated in the AIOM book 2023, with an estimated number of new cancer diagnosis of 390,000 per year [36]. The increased number of potential patients exposed to the risk of VTE could have shown a further benefit in terms of costs in the use of tinzaparin as compared to enoxaparin.

CONCLUSIONS

At current times of heightened need for efficient resource allocation, the adoption of technologies with both clinical relevance and economic benefits for the healthcare system should be promoted. The findings of this study demonstrated that tinzaparin led to cost saving in the management of patients with cancer and VTE over a 3-year period. Additionally, tinzaparin reduced drug wastage, further contributing to the reduction of the economic burden on the healthcare system. Given the limited number of studies on the economic evaluation of therapeutic strategies for the management of patients with cancer and VTE, future research should focus on comparing these therapies with other alternative treatments, as well as conducting similar analyses in other countries to expand the understanding of the economic profile of this therapy.

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Conflict of interest

P.A.C. reports personal consulting fees from Roche and Admirall; payment or honoraria for presentations and/or speakers bureaus from Roche, Sanofi, Novartis, Bayer, and Otsuka.
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