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Cost-utility analysis of propranolol versus corticosteroids in the treatment of proliferating infantile hemangioma in Italy

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Abstract *Objectives* Infantile hemangioma (IH) is the most common childhood benign tumour. A recent phase II/III study has demonstrated the success of propranolol for involution of infantile hemangioma as well as a better efficacy and safety when indirectly compared with corticosteroids. The purpose of this study was to estimate the cost-utility of propranolol (Hemangiol), a new medicinal product and the first to be authorized for this specific paediatric indication, versus corticosteroids in the treatment of proliferating infantile hemangioma requiring systemic therapy.

Methods A life-time mixed decision tree and Markov model was developed to describe the pathway of infants with infantile hemangioma and to assess costs and outcomes in terms of Quality Adjusted Life Years (QALYs) from the perspective of the Italian National Health Service. Clinical inputs were derived from the MA holder's pivotal trial and literature review, and were validated by disease key opinion leaders in Italy. The economic evaluation considered direct medical costs associated with infantile hemangioma, derived from public sources. Atopic dermatitis utilities were used as a proxy for infantile hemangioma. Probabilistic sensitivity analysis was performed to investigate model parameter variabilities.

Results The cumulative costs were €2,399.32 and €1,859.68, while cumulative QALYs were 19.11 and 18.95, respectively for propranolol and corticosteroids (Prednisolone-Deltacortene), corresponding to an incremental cost-utility ratio of €3,372.75 per QALY. Probabilistic sensitivity analysis showed that 94.60% of the 1,000 iterations fall within an a priori €30,000/QALY cost-effectiveness threshold.

Conclusions Propranolol oral solution for the treatment of proliferating infantile hemangioma requiring systemic therapy can be considered cost-effective compared to corticosteroids from the Italian National Health Service (NHS) perspective at a threshold fixed at €30,000/QALY.

Key points for decision makers

- Infantile hemangioma is the most common benign childhood tumour;
- In 12% of cases, infantile hemangioma requires a systemic therapy:
  - Life- or function-threatening hemangioma
  - Ulcerated hemangioma with pain and/or lack of response to simple wound care measures
  - Hemangioma with a risk of permanent scars or disfigurement;
- Propranolol has demonstrated its efficacy and safety in this infantile population;
- Propranolol is the treatment of choice as a first line therapy in IH;
- Propranolol is more effective and better tolerated than corticosteroids [1–5];
- Propanolol oral solution especially developed for paediatric use through a Paediatric Investigation Plan (PIP), is the first drug authorized for the treatment of IH, with a Paediatric Use Marketing Authorization (PUMA);

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- Propranolol for the treatment of proliferating IH requiring systemic therapy can be considered cost-effective compared to corticosteroids from the Italian National Health Service perspective.

1 Introduction

Infantile Hemangioma (IH) is a benign vascular tumour characterized by endothelial cell proliferation of blood vessels in the skin and/or visceral organs. It affects 3% to 10% of all infants under one year of age, resulting in one of the most common benign tumours of infancy [6]. This kind of tumour originates lesions composed of microscopic blood vessels that can be very close to the skin surface, causing the strawberry red colour and the uneven texture. The blood vessels also can be deep in the fat of the skin appearing as a smooth bump under the skin surface [7, 8].

IH shows a peculiar evolution with rapid growth within early infancy, followed by slow involution over the next several years. Indeed, IH appears at birth or within the first few weeks of life (2–4 weeks after birth) and generally grow over the first 6 months of life (proliferation phase), followed by plateau phase and gradual spontaneous involution within 5 to 7 years (involution phase) [8–10].

Several classifications of IH exist. In the past, IHs were classified based on the depth of involved soft tissue in superficial, deep or mixed. Recently, the Guidelines from the Italian Society for the Study of Vascular Anomaliesbase the classification of IH on the distribution and tumours are grouped in focal, multifocal, segmental and eruptive [11].

Most of IHs are small and restricted in area, resulting in no need for treatment since the lesions regress over years without leading to functional impairments or leaving significant residuals. However, about 12% of IHs are more complex and can be associated with severe complications for the patients, therefore requiring treatment [12]. Several complications can derive from growth of IH, ulceration, bleeding, visual defects, airway obstruction, congestive heart failure and, rarely, death [13].

In the absence of registered treatment options, oral corticosteroids were considered first-line therapy of IHs for long time, as recommended in national guidelines. However, data show that corticosteroids only inhibit the tumour growth rather than reduce its size [8, 14]. Moreover, the use of corticosteroids is associated with an unsatisfactory safety profile, causing various and sometimes serious side effects such as interruption of growth, hypertension, glaucoma, obesity, 'moon face' [15].

In 2008, Léauté-Labrèze and colleagues, experts practicing at Children's Hospital in Bordeaux, published their observation that propranolol, a non-selective beta-blocker, had beneficial effects on IH involution. Indeed, they demonstrated that oral propranolol produces not only stabilization but a regression of proliferating hemangioma, without severe side effects [16]. Other studies also demonstrated that oral propranolol provides greater efficacy and higher safety profile than corticosteroids in the treatment of IH [1]. However, the off-label use of the drug resulted in high risks of inappropriate dose in infants, since the therapy was adapted from adult dosage to paediatric populations without an appropriate formulation for young children [2, 3]. Therefore, in order to fill the unmet need in the management of the infants affected by IH, an oral paediatric-specific formulation of propranolol for the treatment of proliferating IH requiring systemic therapy was developed and its efficacy and safety at the most effective dosage demonstrated in a phase 2/3 study leading to a market authorization granted by European Medicines Agency (EMA) [17].

The purpose of the present study was to assess the cost-utility of propranolol (Hemangiol), paediatric use formulation (3.75 mg/mL, oral solution), versus corticosteroids (Prednisolone-Deltacortene) (5.00 mg, tablets) in the treatment of infants with proliferating IH requiring systemic treatment from the Italian NHS perspective.

2 Methods

2.1 Study design

A cost-utility analysis on two treatment strategies [systemic therapy with propranolol oral solution versus systemic therapy with corticosteroids] was conducted to assess the costs and clinical benefits of propranolol in comparison to corticosteroids in the treatment of proliferating IH in Italy. The cost-utility results were reported in terms of incremental cost per QALY gained and expressed by Incremental Cost-Utility Ratio (ICUR).

The results of economic evaluation were expressed in terms of resource consumption and in terms of clinical effectiveness measured by QALYs gained. Therefore the primary outcome was the incremental total costs per QALY that expresses the additional costs implied by adoption of the innovative treatment with propranolol oral solution to gain an additional life year in perfect health. Then, the primary outcome of analysis was expressed in quantitative terms by incremental cost-utility ratio, exploring the cost-utility of propranolol oral solution in the treatment of proliferating IH requiring systemic treatment.

The Italian National Health Service perspective was adopted to evaluate the resource consumption with a lifetime (30 years) time-horizon, by applying a 3.00% discount rate to both costs and health benefits as indicated in Italian guidelines for Economic Evaluation of Health Programs [18].

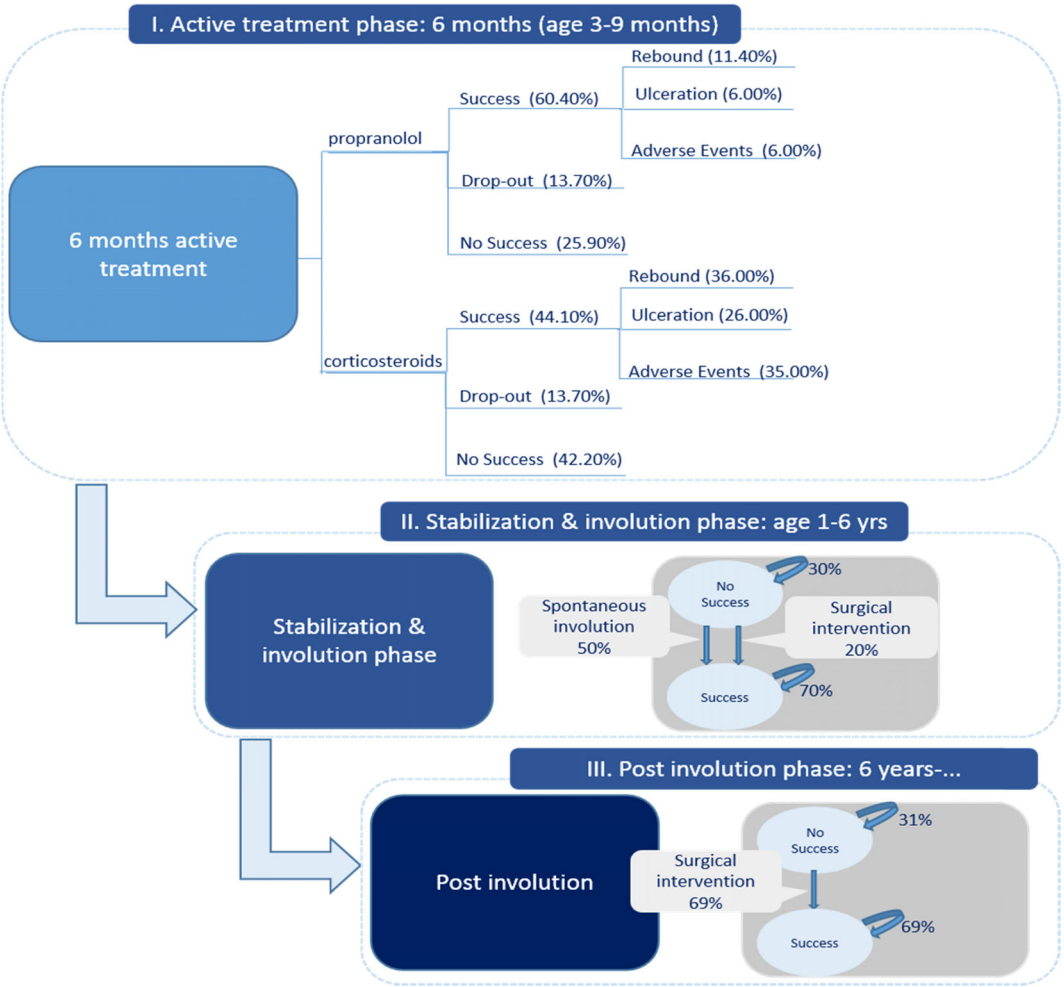

Fig. 1 Structure of decision tree and Markov model of cost-utility analysis

Probabilistic sensitivity analysis was performed to assess the uncertainty around the ICUR.

The probabilistic sensitivity analysis was performed by varying the model input, modelling the transition probability as beta-distributions and the costs as gamma-distributions for 1,000 iterations.

2.2 Model overview

A mixed decision tree—Markov model was developed in order to describe the pathway of infants with proliferating IH requiring systemic treatment. The model, shown in Fig. 1, is divided in 3 macro-phases representing the evolution of IH and the current practice in management of the affected infants: "Active treatment phase", "Stabilization and involution phase" and "Post-involution phase". The Active treatment phase comprises three health states: "Success", defined as a complete or nearly complete resolution of lesions; "No Success", defined as lack of complete or nearly complete resolution of lesions; "Drop-out", defined as the discontinuation of trial treatment. The other two phases comprise two health states: "Success" and "No success".

The first phase represents the proliferation period of hemangioma, in which it is necessary to initiate the active therapy (propranolol or corticosteroids). In this phase the transition from "No Success" to "Success" health state depends on the clinical efficacy of the pharmaceutical therapy (Table 1).

Following the active treatment period, the second phase of the model focuses on spontaneous involution of IH and lasts from the age of 1 year until the age of 6 year, as demonstrated in a retrospective analysis [8]. During the involution phase the model utilizes the transition from "No Success" to "Success" health state which can occur through spontaneous involution of the hemangioma or through active intervention of sequelaes (e.g. surgical resection, laser therapy, or a combination of both). Worsening in the involution phase (transition from "Success" to "No Success") is not to be expected, due to clinical experience.

In the "Post-involution phase" the residual lesions do not resolve spontaneously anymore because the involution pro-

Table 1 Clinical outcomes defining the transition probability between health states during the "Active treatment phase: 6 months (age 3–9 months)"

	Success rate*	Drop-out rate**	Rebound rate***	Ulceration events rate****	Adverse events rate*****
Propranolol[19]	60.40%	13.70%	11.40%	6.00%	6.00%
Corticosteroids[1,3,15,20]	44.10%	13.70%	36.00%	26.00%	35.00%

*Success rate = complete or nearly complete resolution of IH

**Drop-out rate= discontinuation of trial treatment. For corticosteroids is assumed the same of propranolol treatment

***Rebound rate = reintroduction of systemic hemangioma treatment after propranolol/corticosteroids treatment

****Ulceration event rate = complications due to proliferation of hemangioma

*****Adverse events rate = complications related to pharmaceutical therapy

cess is complete. From this time onward, resolution can only occur through active intervention, and it is further assumed that any active treatment will lead to a complete success.

The model was developed with Microsoft Excel.

2.3 Clinical data source

The model was populated with clinical efficacy data which define the transition probability from one health state to another. The clinical efficacy data related to propranolol treatment were obtained from the pivotal head-to-head trial versus placebo published in 2015 in the NEJM [19]. The clinical effectiveness data related to corticosteroids treatment were derived from systematic literature review, more specifically from two meta-analyses of observational studies conducted by Izadpanah et al. and by Bennet et al. [1, 3, 15, 20].

The main clinical outcomes taken into account in the model were success rate (i.e. the complete or nearly complete resolution of IH), drop-out rate (i.e. the discontinuation of trial treatment) and rebound rate (i.e. the reintroduction of systemic hemangioma treatment after therapy with propranolol or corticosteroids). Furthermore, the model incorporates the ulceration (i.e. complications due to proliferation of hemangioma) and adverse events (i.e. complications related to pharmaceutical therapy) related to the different therapeutic approaches. Table 1 indicates all main clinical outcomes that define the transition probability between health states.

Moreover, the model assumes that during the "Stabilization and involution phase" in 50% of patients, for whom pharmacological treatment was not completely effective, hemangioma spontaneously involutes [21, 22]. Whereas in 20% of patients an active intervention, like laser treatment, surgery or a combination of both, is necessary to remove residual hemangioma [22]. Table 2 shows treatment modality distribution for residual lesions in "Stabilization and involution phase" and in "Post-involution phase". In the "Post-involution phase" the model assumes that residual lesions were presented in 69% of patients [23].

Table 2 Treatment modality distribution for residual lesions in "Involution & stabilization phase" and in "Post-involution phase"

	Percentage patients receiving
Surgery resection	40.00%
Laser therapy	47.50%
Combination of two treatment*	12.50%

*Combination = Surgery resection + Laser therapy

2.4 Utilities

Since no utility value was estimated for the condition of IH (corresponding to the health state "No Success") or is available in literature, the utility estimate for atopic dermatitis was selected as a proxy for IH utilities. The used utility data were extrapolated from a work done by Monti at al. that estimated the utility in an Italian sample of children (aged between 1–12 years) affected by atopic dermatitis using the Infants Dermatitis Quality of Life Index (IDQoL) and the Children's Dermatology Life Quality Index (CDLQI).[1] In accordance with results of this study, the level of utility associated with a patient affected by IH, using atopic dermatitis as proxy, was set equal to 0.76 (adjusted on scale from 0 to 1) during the proliferative phase and modelled according to the evolution of the disease [24].

Moreover, in the estimation of the quality of life, the decrease of utility due to the use of corticosteroids was taken into account. Indeed, the administration of these drugs has a greater impact on utility perceived by patients and their families than the administration of propranolol, due to the higher incidence of toxicity and side effects of corticosteroids [1]. The decrease of utility was quantified equal to 3%, in accordance with a study conducted in UK that assessed the Utility

[1] In particular, the mothers filled the IDQoL questionnaire for children age 1–4 years. While, children age 5–12 years completed the CDLQI questionnaire by themselves and in some cases with the help of their mother.

in patients with atopic dermatitis treated with corticosteroids compared to a less toxic treatment [25].

2.5 Resource use and costs

The evaluation of resource consumption was conducted on the basis of the clinical pathway of infants, modelled in the decision model and based on interviews done with key opinion leaders experienced in the treatment of IH. The interviews were focused on dosage and length of pharmaceutical therapy, treatment setting (outpatient, day-hospital or inpatient care) and the frequency and type of monitoring visits in follow-up plan.

The economic evaluation considered only direct medical costs associated with drug acquisition, hospital admissions and outpatient visits. The direct non-medical costs such as travelling; waiting periods and indirect costs were not included in the analysis according to the Italian National Health Service perspective adopted.

The estimation of the pharmaceutical costs was performed on base of ex-factory price of the respective drugs, as this represents the maximum cost for the public structures. The cost of propranolol was fixed at €180.50 (3.75 mg/mL, oral solution for paediatric use, bottle of 120 mL. The cost of corticosteroids was obtained from "Compendio Farmaceutico Telematico-Farmadati 2013" equivalent to €1.04 (5.00 mg, tablets). While the dosage and the duration of therapy were determined according to the data collected in the interviews with expert opinion.

The resource consumption for hospitalization was estimated following the DRG-based reimbursement system, using version 24 of DRG-Grouper and the national tariffs established by Ministerial Decree of 18th October, 2012 [26]. The hospital admission for the first administration of the drug, necessary for both evaluated clinical pathways, was coded by DRG 284 "*Minor skin disorders without complications*" to which a tariff equal to €153.00 in day hospital setting is associated [26]. The first administration of the therapy was considered in day hospital setting also for corticosteroids according to the opinion of Clinical Experts of three Reference National Centres of this pathology, based in northern, central and southern Italy, considering the distinctive features of patient under one year of age and the well-known adverse event related to the corticosteroids treatment. The hospitalization for the surgical resection of residual lesions was coded by DRG 120 "*Other acts on cardiovascular system*" to which a tariff equal to €1,898.00 in day hospital setting is associated [24]. While the estimate of the cost related to laser therapy to remove residual lesions was performed according to DRG 270 "*Other acts on skin*" and to the number of sessions necessary to remove the lesions (requiring 3 sessions on average). The total cost associated with laser therapy resulted in €3,297.00 [24].

The resources associated with outpatient visits for the follow-up of the pharmaceutical treatment were estimated on basis of National Outpatient Tariffs established by Ministerial Decree of 18th October, 2012 [26]. In particular, the follow-up plan for the patients treated with propranolol involves a dermatological visit scheduled monthly, to which a tariff equal to €20.66 is associated. While for the patients treated with corticosteroids the follow-up plan is more intensive, consisting of a dermatological and a general outpatient visit conducted monthly, to which a tariff equal to €20.66 for both visits is associated.

The model also included the representation of ulceration and adverse events resulting from pharmaceutical therapies (the ulceration is not generally related to the therapy but it is a potential complication of IH most frequently during the 3–4th month, potentially requiring laser and weekly outpatient visits to prevent infection). The costs associated with treatment of ulceration were estimated with reference to the current clinical practice, that involves two sessions of laser treatment performed in day-hospital setting and coded by DRG 270 "Other skin procedure without complications", to which a tariff of €1,099.00 is associated. In succession, four dermatological outpatient visits are performed to monitor evolution of the ulceration. On the base of this information, the total cost of managing ulceration was estimated at €2,280.64.

The costs associated with adverse events related to propranolol treatment were quantified assuming that a hospital admission in day hospital setting is necessary to treat the complication. This hospitalization was coded by DRG 284 "*Minor skin disorders without complications*," to which a tariff equal to €153.00 is associated. For the management of complications resulting from the use of corticosteroids the costs were estimated by the average of costs related to the most frequent adverse events, like: hypertension caused by corticosteroids, interruption of growth, glaucoma, obesity, 'moon face' [15]. This estimate was conducted taking into consideration additional costs for pharmaceutical treatments, hospital admissions and outpatient visits, and amounts to €799.49. Table 3 reports details about all cost items considered in the model associated with the two treatment scenarios.

2.6 Sensitivity analysis

A probabilistic sensitivity analysis was conducted to assess the uncertainty around the ICUR and the probability to be cost-effective at a given cost per QALYs threshold.

In the probabilistic sensitivity analysis the transition probability was modelled as beta-distributions, while the costs were modelled as gamma-distributions, in accordance with method of moments estimation [27].

Table 3 Cost and resource consumption

	Propranolol (Hemangiol)	Corticosteroids (Prednisolone-Deltacortene)
Pharmaceutical therapy costs		
Dosage	1° week at 1.00 mg/kg/day 2° week at 2.00 mg/kg/day 5.5 months at 3.00 mg/kg/day	3 courses of 20 days each at 1,2mg/Kg/die + gastro protector (Ranitidina) at 7.50 mg/kg/day
Length of therapy	6 months	3 courses of 20 days
Costs[*]	€1,510.79	€18.88
Hospitalization costs for the first administration of the drug		
DRG coded	DRG 284 "*Minor skin disorders without complications*"	D RG 284 "*Minor skin disorders without complications*"
Tariff	€153.00	€153.00
Outpatient visit costs		
Type of visit	Dermatological visit—code 89.7	General + Dermatological visit—code 89.7
Tariff	€20.66	€20.66
Number of visits	8[**]	12
Costs	€165.28	€247.92
Adverse events costs	€153.00	€799.49
Ulceration events costs		
DRG coded	DRG 270 "*Other skin procedure without complications*"	
Tariff	€1,099.00	
Type of visit	Dermatological visit—code 89.7	
Tariff	€20.66	
Number of visits	4	
Costs	€2,280.64	
Surgical resection costs		
DRG coded	DRG 120 "*Other acts on cardiovascular system*"	
Tariff	€1,898.00	
Laser therapy costs		
DRG coded	DRG 270 "*Other skin procedure without complications*"	
Tariff	€1,099.00	
Number of session	3	
Costs	€3,297.00	

[*]The estimate of pharmaceutical therapy costs was performed taking into account a average body weight equal to 7.24 Kg

[**]The total number of visits is 8 to take into account of 2 outpatient visits to perform the titration of the dosage

3 Results

Total costs, including pharmaceutical and healthcare costs (outpatient and inpatient costs), related to propranolol treatment were greater than total costs related to corticosteroids treatment: €2,399.32 versus €1,859.68. This major resources consumption was due to price difference between the propranolol drug and corticosteroids (€180.50 versus €1.04) and due to dosage and duration of the pharmaceutical therapies, 3 mg/Kg/day for 6 months for propranolol and 1.20 mg/Kg day for 3 courses of 20 days for corticosteroids.

The economic analysis showed that healthcare costs associated with propranolol were lower than costs associated with corticosteroids (€994.29 versus €1,842.12, respectively) (Table 4). However, some Hospitals may use a dif-

Table 4 Summary of the final results*

	Propranolol			Corticosteroids		
	Base case	p 2,5	p 97,5	Base case	p 2,5	p 97,5
Pharmaceutical costs	€1,405.03	€1,350.23	€1,453.47	€17.56	€16.88	€18.14
Healthcare costs	€994.29	€709.01	€1,320.26	€1,842.12	€1,432.84	€2,082.19
Total costs	€2,399.32	€2,059.24	€2,773.73	€1,859.68	€1,449.72	€2,100.33
Total QALYs	19.11	18.80	19.47	18.95	18.60	19.33

	Base case	p 2,5	p 97,5
ICUR	€3,372.75/QALY	€3,047.60/QALY	€4.810.00/QALY

*The results were based on 30 year lifetime and 3% of discount rate for both costs and benefits

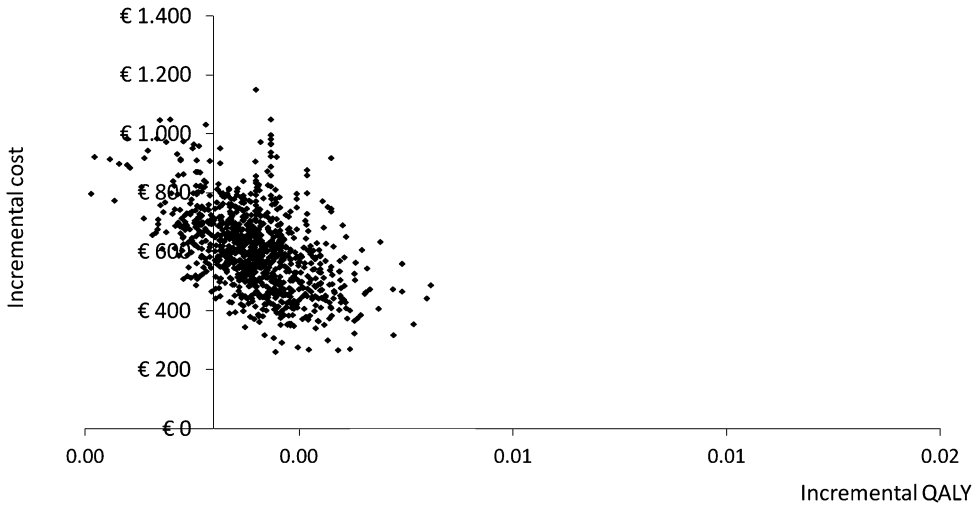

Fig. 2 Cost-effectiveness plan (PSA)

ferent setting for the first administration for corticosteroids (such as outpatient setting instead of day hospital), with a consequently possible reduction of the costs of the treatment.

Nevertheless, not taking into account the hospitalization for the first administration of the drug that is common for the two scenarios, a greater number of inpatient admissions and outpatient visits was associated with the patients treated with corticosteroids. Effectively the adoption of corticosteroids in the treatment of proliferating IH implies a more intensive follow-up plan with an additional outpatient visit (code 89.7-outpatient visit) compared to propranolol, and a major numbers of hospitalizations to manage adverse events and occurrence of ulceration.

The cumulative QALYs associated with propranolol oral solution were equal to 19.11, while the cumulative QALYs associated with corticosteroids were equal to 18.95.

The incremental costs related to the adoption of propranolol oral solution in the treatment of proliferating IH were equal to €539.64, while the incremental QALYS amounted to 0.16, corresponding to an ICUR of €3,372.75 per QALY gained.

The probabilistic sensitivity analysis demonstrated that the model is robust and accurate to the variation of the inputs, as showed on the cost-effectiveness plan and on acceptability curve in Figs. 2 and 3. The results suggested that 94.60% of the 1,000 iterations fell within a €30,000 cost-effectiveness threshold considered acceptable for a marginal unit of effectiveness.

Table 4 resumes the final results of the economic evaluation including the PSA results.

4 Discussion

IH is the most common vascular tumour of childhood that develops due to abnormal changes in angiogenesis [7]. For long time the therapy with corticosteroids was considered as the first line treatment, even if their use was off-label and only limited clinical evidence was available, until 2008, when the publication by Léauté Labrèze et al. showed the efficacy of propranolol in patients affected by IH [14, 16]. Following this discovery several publications, including meta-analyses and randomized clinical trials, have confirmed the

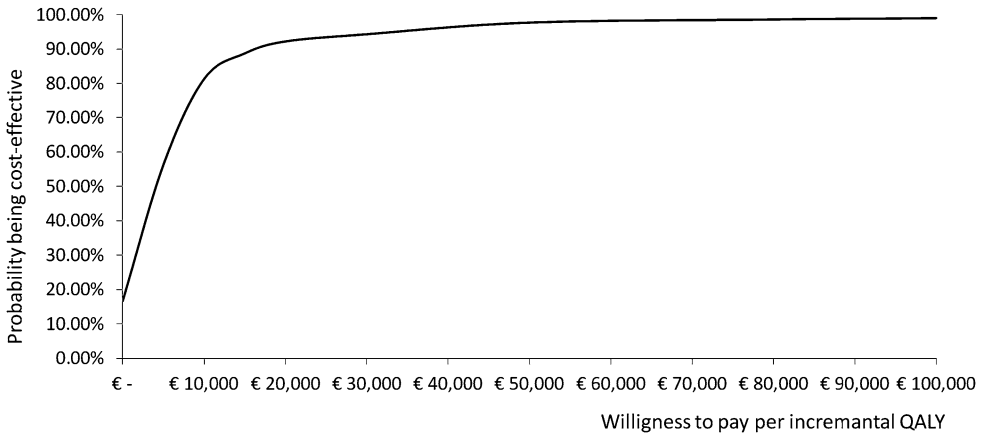

Fig. 3 Acceptability curve

efficacy of propranolol in patients with IH and have demonstrated that is a more effective and better tolerated treatment than corticosteroids, with faster onset of action [1]. The scientific community has acknowledged the treatment with propranolol as the best treatment available for the resolution of infantile haemangiomas [4].

In order to cover these unmet needs, an oral formulation with propranolol, specifically for use in infants, was developed in compliance with the formulation guidelines for paediatric drugs and a full clinical development complying with a Paediatric Investigation Plan (PIP) has been conducted, leading to a Paediatric Use Marketing Authorization (PUMA) granted by EMA [17].

No economic analysis of propranolol in the treatment of IH has previously been reported. Therefore, the authors considered it significant to carry out this study, as first economic evaluation of treatment with propranolol in form of a registered medicinal product, establishing the economic value of this therapy, in addition to evidence of safety and efficacy. In particular the results obtained from the model showed that implementing propranolol oral solutions in the treatment of proliferating IH requiring systemic treatment can significantly increase rate of resolution of the lesions on the long term. Even if implementing propranolol implies additional cost for the introduction of the therapeutic treatment, this therapy can be considered cost-effective from the Italian National Health Service perspective, even though in Italy a cost-effectiveness threshold is not clearly stated by institutional body. However, in literature we can find, a range of values of cost-effectiveness ratio variable from €17,907 per QALY gained [28] to €25,000–€40,000 per QALY gained [18]. Moreover, a threshold around €30,000/QALY is commonly accepted and applied in other health economic evaluations [29, 30].

Corticosteroids were included as comparator in this analysis because they were considered as standard of care in some clinical settings, until discovery of propranolol pharmacological effect in IH. Moreover they are only registered for treatment of severe forms of hemangiomas in infants in two countries in Europe (France and Germany). The most part of publications use corticosteroids, considered as standard of care, as comparator versus propranolol such as the recent randomized clinical trial of Bauman et al. that compares the safety profile of oral propranolol and oral prednisolone in the treatment of IH published in 2014 [3].

These results can be considered robust and accurate although they come from a Markov model that is a simulation and a simplification of real world. For this reason some assumptions can be necessary that may influence the final results. In this regard some limitations can be identified in the model.

The first is related to the absence of head-to-head data for a direct comparison propranolol versus corticosteroids. Indeed, the data for propranolol efficacy were extracted from the MA holder's pivotal trial, while data for corticosteroid efficacy were based on a meta-analysis of observational studies by Izadpanah expressed in terms of relative efficacy respect efficacy of propranolol.

Another limitation of the study is represented by the estimate of utility for the patients affected by IH, using atopic dermatitis as a proxy for IH. This kind of choice was made due to lack of published studies investigating the utility values in order to estimate the quality of life. Even if the use of atopic dermatitis as proxy is an assumption that potentially influences the final results, this choice was validated by a Focus Group composed by five Clinicians experts in the treatment of IH, representatives of five Italian Regions and two Pharmacoeconomists that considered it appropriate since atopic dermatitis is a pathology with many similarities to the Infantile Hemangioma.

Indeed the atopic dermatitis, especially in its more severe form, causes strong itching and soreness that are source of sleeplessness and can subsequently lead to tiredness and mood changes, impacting significantly in quality of life like IH [31]. Moreover the data regarding the utility used in the economic evaluation are completely referred to Italian context [24].

5 Conclusion

The present finding suggests that the implementation of propranolol oral solution (in the treatment of IH requiring a systemic therapy) results to be a cost-effective therapy compared with corticosteroids from the Italian National Health Service perspective.

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