Chemotherapy: Open Access
ISSN: 2167-7700

Habibian and Dehghani, Chemo Open Access
2016, 5:4
DOI: 10.4172/2167-7700.1000217

Research Article Open Access

IEV versus ESHAP for Treatment of the Patients with Relapsed/Refractory Hodgkin and Non-Hodgkin's Lymphoma in Iran: A Cost-Effectiveness Analysis

Mostafa Habibian[*1] **and Mehdi dehghani**[2]

[1]*Master of Health Economics, School of Management and Information Sciences, Iran University of Medical Sciences, Tehran, Iran*

[2]*Hematology and oncology ward, hematology Research Center, Shiraz University of Medical Sciences, Shiraz, Iran*

[*]**Corresponding author:** Mostafa Habibian, Master of Health Economics, School of Management and Information Sciences, Iran University of Medical Sciences, Tehran, Iran, Tel: 00989013766363; E-mail: m_habibyan@yahoo.com

Received date: August 22, 2016; **Accepted date:** October 15, 2016; **Published date:** October 24, 2016

Abstract

Background: The aim of this study was to perform cost-effectiveness Analysis of IEV versus ESHAP chemotherapy regimen in patients with Lymphoma in Iran.

Materials and Methods: Our study used a cross-sectional design done as a double-blind study of 65 patients suffering from relapsed/refractory Hodgkin and non-Hodgkin's Lymphoma in Amir Oncology Hospital in Shiraz, in the south of Iran. The costs were included medical and non-medical direct costs and indirect costs. Effectiveness was reported in patient records and it was categorized into complete response, partial response and non- response

Results: The direct cost in IEV and ESHAP regimens 32159.87 and 69,143.72 respectively. In IEV arm, 53% of the patients with Hodgkin Lymphoma achieved complete response (CRs) and 35% a partial response (PRs). The overall response rate (CRs & PRs) was 88.2%. But in ESHAP arm, the overall response rate was 69.2%, 43.3% of patients achieved a complete response and 27% a partial response.

Conclusions: The results showed that IEV versus ESHAP was dominant in the treatment of patients with lymphoma. Also, ICER was -$109749.23 (using IEV saves $109749.23 per each additional effectiveness)

Keywords: Hodgkin lymphoma, Non-Hodgkin's Lymphoma, Cost, IEV, ESHAP

Introduction

In Iran, 2009, the total number of cancer cases reported were 74,067 people, 55.58% in males and 44.42% in females and the age-standardized incidence rate of relapsed/refractory NHL & HL cancer is 4.57 among men in Fars Province [1]. Meantime, the therapeutic approach of relapsed/refractory NHL&HL is a major challenge in the medicine [2].

Considering that, economic burden is measured by three costs domains: (a) Medical direct costs; (b) Non-medical direct costs; and (c) Indirect costs [3], the National Institutes of Health (NIH) estimates that the total costs of cancer in 2009 were $216.6 billion: $86.6 billion for direct medical costs (total of all health expenditures) and $130.0 billion for indirect mortality costs (cost of lost productivity due to premature death) [4]. After primary treatment for HL and NHL, 10% to 15%-20% of patients with early-stage disease will experience relapse, and 35% to 40% of patients with advanced stage at diagnosis will relapse [5,6]. For those who are refractory to the first-line therapy or relapse at a later time need additional therapy [7]. According to what was said, the type of response (effectiveness) in these patients is important.

The treatment of relapsed/refractory lymphoma with conventional and standard therapy such as chemotherapy or radiotherapy is not a satisfactory treatment [2] Chemotherapy for cancer of the lymphoma nodes is often composed of several drugs that are used in a treatment program [8]. One of these methods is ESHAP regimen, a combination of the chemotherapeutic drugs Etoposide (40 mg/m^2), methylprednisolone (500 mg/m^2), high-dose Cytarabine (2 g/m^2) and Cisplatin (25 mg/m^2) [9], and has been shown to be active against refractory/relapsed lymphoma [7]. Another method is IEV, a combination of three drugs Ifosfamide (2,500 mg/m^2), Epirubicin (100 mg/m^2), and Etoposide (150 mg/m^2). These patients responded to chemotherapy in three forms: complete response, partialresponse, non-response [10].

To our knowledge, no studies has presented information on the cost-effectiveness of the two regimens but in terms of effectiveness, Choi et al. and Wang et al. showed ESHAP regimen is effective in patients with relapsed NHL. Also Mashhadi et al. and Zinzani et al. showed IEV regimen is effective in patients with relapsed/refractory NHL&HL [7,11-13].

Materials and methods

This study is a cost-effectiveness analysis. Our study used a cross-sectional design done as a double-blind study of 65 patients suffering from relapsed/refractory Hodgkin and non-Hodgkin's Lymphoma with a mix of urban and rural patients, in Amir Oncology Hospitalin Shiraz, Iran. The study was conducted on patients who were selected by goal-oriented sampling, from April 2013 to April 2014.

It should be noted that we developed interviews for measuring costs that result from relapsed/refractory Hodgkin and non-Hodgkin's

Lymphoma cancer for the patient or a family member. The data collection form was used during the interview after 6 months of follow-up at the last session (6^{th}) of chemotherapy for each participant. The data was collected in this part of the study by interviewing at one month after the last chemotherapy because according to oncology experts, drugs effect emerges one month after chemotherapy. At this stage, the patient number was recorded in order to collect the type of their treatment regimen and drugs effect. All participants provided an informed consent.

Data was divided into two parts, effectiveness and costs. The costs were identified from the social perspective and were measured for a period of 6 months and they included costs associated with medical and non-medical direct costs and indirect costs. In this study, a data collection form was used to collect data; it consisted of two parts. The first part included demographic data of the patients and in the second section, data were obtained about medical direct costs [the therapy and pharmaceutical costs, diagnostic and laboratory (lab, radiology, MRI etc.)], and non-medical direct costs (the cost of traveling, lodging, phone, auxiliary equipment, special diet during chemotherapy). Also, indirect costs calculated using the Human Capital Approach (time spent by the patients and the patient's accompany multiplied by their monthly income). We assigned $0 to any patients who received a specific regimen but who did not experience costs related to it. On the other side, the study period was one year, so use the discount rate is not required for adjustment time. The total medical costs for each patient in each study arm were estimated as the sum of all cost categories and were converted to 2014 US dollars.

Effectiveness was reported in patient records and was categorized into complete response (CR: the complete disappearance of signs and symptoms due to lymphoma and maintained for at least 6 weeks),partial response (PR: was defined as a reduction of at least 50% in the product of the two largest perpendicular diameters of all measurable lesions for a duration of a least 6 weeks) and progression of disease (PD) or non- response (was used where there was unequivocal evidence of advancing disease, despite continuation of the treatment) [10].

All of the patients (with relapsed/refractory HL&NHL) underwent one of the two methods: IEV and ESHAP and all those who were admitted to treat lymphoma, during the year, entered in the study, 65 patients. The number of patients in studies conducted by Rodriguez et al, Wang et al, Choi et al, Zinzani et al. and Mashhadi et al. were, respectively, Ninety-two, Thirty-two, Forty, Sixty- two and Twenty-four. So, sampling was not necessary but the patients were divided in two groups after a physician had chosen their types of regimen. This makes it closer to routine practice in clinical setting. However, the patients and researchers were blind to this allocation. When using these two methods, courses were repeated every 21 days about 3-4 times [7].

The model was structured as a decision tree, comparing IEV versus ESHAP as therapy methods over a maximum 1-year time horizon. So, we did not follow patients after response to the two drugs. A short time horizon is a limitation in our study, so it is recommended that long-term study be conducted in future. The structure of the model is shown in Figure 1. By the decision tree, the expected costs and effectiveness were calculated.

The outcome measure for this analysis was the incremental cost-effectiveness ratio (ICER), defined as the incremental cost divided by the number of effectiveness saved (response to the drugs). To increase the accuracy of the study, one-way deterministic sensitivity analysis (Tornado Diagram) and probabilistic sensitivity analyzes were performed. For the one-way sensitivity analyses, we allowed values to vary ± 20% (the upper and lower bounds, corresponded to similar studies) of base line for chemotherapy, hospitalization and traveling costs, time spent by the patient for the two drugs.

The probabilistic sensitivity analysis was performed using a Monte Carlo simulation using TreeAge Prosoftware. For this analysis, 10,000 simulated trials were run, where each input was sampled at random from probability distribution functions assigned to each variable. In all of figures, in both drugs, the first branch is showed with "1" and the second branch, "2".

Results

Based on the results of the present study, among the 65 patients studied, 66.1% were male, 67.7% were married, 60% were aged less than 40 years and all patients had insurance. Also 72% of the patients and 93% of the patient's accompany had less than $400 income monthly. In addition, the mean length of stay per each time of chemotherapy was 3 days in the IEV arm and 5 days in the ESHAP arm. The results are shown in Tables 1A and 1B.

Type of lymphoma	Type of treatment protocol	Number of Patients	The average length of stay per each time chemotherapy
Hodgkin	IEV	17	3 days
	ESHAP	26	5 days
non-Hodgkin	IEV	10	3 days
	ESHAP	12	5 days
total	IEV	27	3 days
	ESHAP	38	5 days

Table 1A: Frequency based on the type of chemotherapy regimen.

As seen in Table 2A, in both IEV and ESHAP arms, the medical direct costs was the highest (32159.87 and $69,143.72, respectively) and the non-medical direct costs was minimum (6400.89 and $7,918.85, respectively).

As seen in Table 2B, the cost of chemotherapy in the IEV arm was $13201.24 that is the highest type of medical direct costs. Also, in the ESHAP arm, the cost of chemotherapy was $32943.08 and it was the highest medical direct costs. Traveling costs and indirect costs of the patients were respectively the highest type of non-medical direct costs and indirect costs in both arms. (In the IEV arm, 4037.14 and $15179.65 and in the ESHAP arm 3980.62 and $13362.94, respectively).

According to Table 3, in IEV arm, 53% of the patients with Hodgkin Lymphoma achieved complete response and 35% a partial response. The overall response rate (CRs & PRs) was 88.2%. But in ESHAP arm, the overall response rate was 69.2%, 43.3% of patients achieved a complete response and 27% a partial response. However, in IEV arm, 40%of the patients with Non-Hodgkin's achieved complete response and 40% a partial response. The overall response rate (CRs & PRs) was 80%. But in ESHAP arm complete response, partial response and overall response rate were 25%, 41.7%and 66.6%, respectively.

Variable		Number	Percent
Sex	Man	43	66.1
	Woman	22	33.9
	Total	65	100
age	<40	39	60
	>40	26	40
	Total	65	100
Marital Status	Married	44	67.7
	Single	21	32.3
	Total	65	100
Education	Collegiate Education	28	57
	Non- Collegiate Education	37	43
	Total	65	100
Monthly income	<$400	47	72
of patients	≥ $400	18	28
	Total	65	100
Monthly income	<$400	60	93
of patient's accompany	≥ $400	5	7
	Total	65	100
Insurance	Yes	65	100
	No	0	0

Table 1B: Frequency based on the demographic characteristics of lymphoma's patients.

Type of treatment protocol	IEV	ESHAP	p-value
Costs mean			
Medical direct costs	32159.87	69,143.72	0.0001
Non-medical direct costs	6400.89	7,918.85	0.545
Indirect costs	16152.6	17,359.71	0.249
Total	54713.36	94,422.29	0.123

Table 2A: The cost of cancer patients with lymph node based on the type of costs.

Strategy	Costs components	Mean ± SD
ESHAP	**Medical direct costs:**	69,143.72 (73%)
	Medication	32943.08 (35%)
	Hospitalization	9931.37 (11%)
	Sonography	775.13 (1%)

	Radiology	2751.31 (3%)
	MRI	621.72 (1%)
	Surgical Cost	4299.56 (5%)
	Laboratory Tests	8800.97 (9%)
	CT-SCAN	2955.19 (3%)
	Visits	998.79 (1%)
	Other	5066.61 (5%)
	Non-medical direct costs:	7,918.85 (8%)
	Traveling	3980.62 (4%)
	Lodging	2111.43 (2%)
	Phone	890.19 (1%)
	Auxiliary Equipment	68.63 (0.07%)
	Special diet	867.99 (1%)
	Indirect costs:	17,359.71 (18%)
	Time spent by the patient	13362.94 (14%)
	Time spent by the patient's accompany	3996.77 (4%)
	Total:	94422.29
IEV	**Medical direct costs:**	32159.87 (59%)
	Medication	13201.45 (24%)
	Hospitalization	3451.76 (6%)
	Sonography	557.13 (1%)
	Radiology	1441.26 (3%)
	MRI	282.60 (1%)
	Surgical Cost	4339.93 (8%)
	Laboratory Tests	3863.54 (7%)
	CT-SCAN	1929.75 (4%)
	Visits	609.61 (1%)
	Other	2482.84 (5%)
	Non-medical direct costs:	6400.89 (11%)
	Traveling	4037.14 (7%)
	Lodging	1320.15 (2%)
	Phone	680.26 (1%)
	Auxiliary Equipment	129.19 (0.2%)
	Special diet	234.15 (0.4%)
	Indirect costs:	16152.60 (30%)
	Time spent by the patient	15179.65 (28%)

	Time spent by the patient's accompany	972.95 (2%)
	Total:	54713.36

Table 2B: The cost components of IEV and ESHAP in lymphatic cancer as included in the analysis.

Type of lymphoma	Type of treatment protocol	Complete response	Partial response	Non- response	Overall response rate
Hodgkin	IEV	9 (53%)	6 (35%)	2 (12%)	88.2
	ESHAP	11 (42.3%)	7 (27%)	8 (30.7%)	69.2
non-Hodgkin	IEV	4 (40%)	4 (40%)	2 (20%)	80
	ESHAP	3 (25%)	5 (41.7%)	4 (33.3%)	66.6
total	IEV	13 (48.2%)	10 (37%)	4 (14.8%)	85.2
	ESHAP	14 (37%)	12 (31.5%)	12 (31.5%)	68.4

Table 3: The effectiveness of IEV versus ESHAPin refractory/relapsed Hodgkin and non-Hodgkin's Lymphoma.

As seen in Figure 1A, the results of decision tree showed that in the IEV arm, the expected cost was $39,297 and the expected effectiveness was 0.74 and in the ESHAP arm, the expected cost was $59,074 and the expected effectiveness was 0.56. Thus, as shown in the Figure 1B, IEV was dominant as compared to ESHAP.

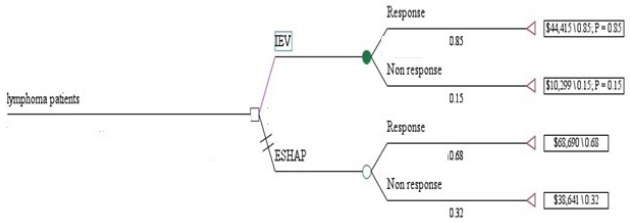

Figure 1A: Results of the decision tree comparing IEV versus ESHAP. These patients responded to chemotherapy in two forms: response(CRs & PRs) and non-response in both arms. Total costs (Table 2B) and effectiveness showed in front of each branch and probabilities on each of them.

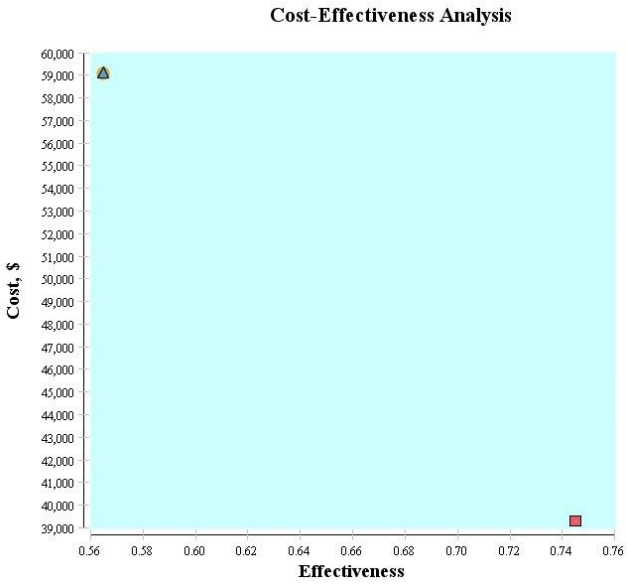

Figure 1B: Cost-effectiveness analysis of IEV versus ESHAP. Effectiveness showed on X-Axis and Costs on Y- Axis. The IEV regimen (Square) has high effectiveness with low cost but the ESHAP regimen has high low effectiveness with high cost.

Sensitivity Analysis

The results of the one-way sensitivity analysis are shown in the tornado diagram in Figure 2, which depicts graphically how variations in each input affect the outcome. The tornado diagram is stacked in order of decreasing width, indicating that variations in inputs near the top (Medication costs) have the greatest effect on the outcome, while variations in inputs near the bottom (hospitalization rate and Traveling costs) have relatively small effects on the outcome.

For the probabilistic sensitivity analysis, the results of the MonteCarlo simulations are shown in the scatterplot in Figure 3. Each point represents one of the 1,000 trials run where each input was assigned a random value according to its probability distribution function. Results showed in 97% of the iterations, IEV was a dominant strategy.

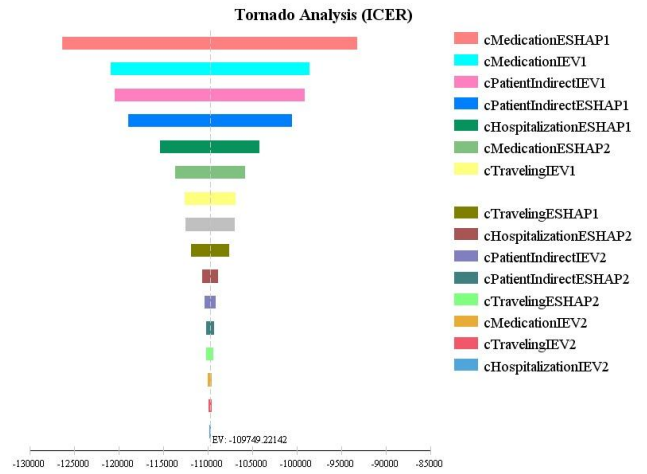

Figure 2: Results of One-Way Sensitivity Analysis (Tornado Diagram). The graph is called a tornado diagram because the bars are arranged in order, with the widest bar (potentially the most critical uncertainty) at the top and the narrowest bar at the bottom. The letter C, in the beginning of each word, represents the costs.

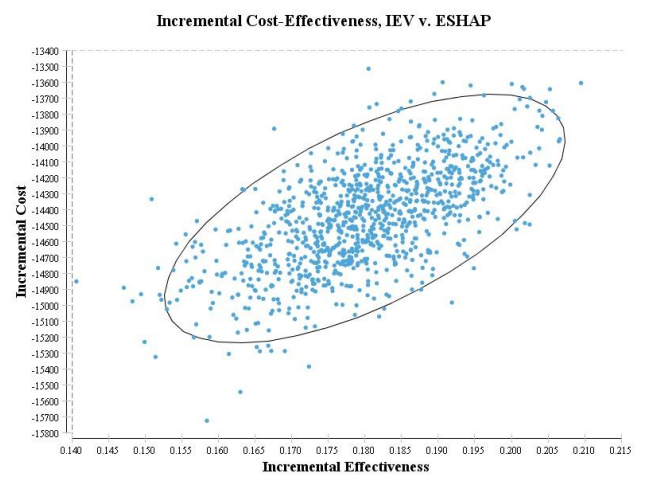

Figure 3: Incremental cost-effectiveness plane. Incremental Effectiveness showed on X-Axis and Incremental Coston Y-Axis. Each point represents one of the 1,000 trials run where each input was assigned a random value according toits probability distribution function. Results showed in 97% of the iterations, IEV was a dominant strategy because of high effectiveness with low cost.

Discussion

The costs and consequences of interventions and programs are compared in economic evaluation for the optimal use of scarce resources; therefore, the aim of this study was to perform a cost-effectiveness analysis of IEV versus ESHAP in patients with lymphoma. To our knowledge, this is first cost-effectiveness analysis in patients with lymphoma in Iran.

Considering that, lymphoma is among the ten most common cancers [14] and also cancer is the third leading cause of death in the country [15], the discussion about the effectiveness and costs associated with them is very important. Twenty-two patients with refractory/relapsed non-Hodgkin's lymphoma and Forty-three patients with refractory/relapsed Hodgkin's lymphoma were enrolled in this study. The number of patients in studies conducted by Rodriguez et al., Wang et al., Choi et al., Zinzani et al., and Mashhadi et al., were respectively, Ninety-two, Thirty-two, Forty and Sixty-two and Twenty four[7,11-13,16]. Sixty-five patients were enrolled in this study.

Based on the results, the direct cost of treatment in IEV and ESHAP arms were 32159.87 and $69,143.72, respectively and the difference was significant (p value=0.0001). Also, the cost of chemotherapy was $32943.08 in the ESHAP arm; it is 35% of total costs. However, the cost of chemotherapy was $13201.45 in the IEV arm, which is 24% of total costs. The Costs, especially chemotherapy drugs and medical direct costs were higher because of the higher cost of chemotherapy. Also, earlier discharge of patients with lymphoma would lead to reducing the length of stay and the medical direct costs [17-23]. To our knowledge, no study has been conducted on the cost of these drugs (IEV & ESHAP) in patients with lymphoma and certainly this is the first study in terms of costs of IEV & ESHAP in Iran.

Also, based on the results, 53% of the patients with Hodgkin Lymphoma in IEV arm, attained complete response and 35% had partial response. The overall response rate (CRs & PRs) was 88.2%. But in ESHAP arm complete response, partial response and overall response rate were 43.3%, 27% and 69.2%, respectively. However, 40% of the patients with Non-Hodgkin's in IEV arm, attained complete response and 40% had partial response. The overall response rate (CRs & PRs) was 80%. But in ESHAP arm complete response, partial response and overall response rate were 25%, 41.7% and 66.6%, respectively. As mentioned, it's not done a cost-effectiveness analysis of the two drugs. So, we reviewed studies that they have been done in relation to effectiveness of the drugs. All studies are consistent with our study in terms of effectiveness. Rodriguez et al showed that MINE-ESHAP is an effective salvage strategy for patients with recurrent lymphoma. In their study the response rate to MINE-ESHAP was 69% (48% CRs and 21% PR [16]). Also, Wang et al showed that ESHAP is an active and tolerable regimen in patients with relapsed/refractory Non-Hodgkin's lymphoma, but the duration of remission is brief and without significant impact on survival. In their study ten patients attained CR and seven had partial remission (PR) and the overall response rate was 53.1% [13]. Choi et al. in their study on ESHAP concluded that in relapsed/refractory NHL patients, the overall response rate was 70%; 22.5% of patients achieved a CR and 47.5% a PR [11]. According to a study conducted by Zinzani et al. IEV is effective in patients with lymphoma, so that 36% achieved a CR and 28% PR, giving an overall response rate of 64% in patients with NHL and 66% obtained CR and 34% PR, giving an overall response rate of 100% in patients with HL. In other study they showed that the overall and CR rates were, respectively, 77% and 32% in NHL and 81% and 45% in HL [10,23].

Based on the results of this study and comparison with other studies, in relation to effectiveness, it was discovered that the overall response rate is high in both regimes and these findings have many similarities with our study about the number of patients and the response.

Although, the nonrandomized and uncontrolled design of the study may cause bias in our results, this makes it closer to routine practice in

clinical setting. Due to the lack of data on costs and effectiveness in longer-term, the possibility of obtaining full effect of these treatments over life time is limited that this restricts the generalizability of our findings. Also, the small number of participants and short time horizon may limit the generalization of the results to other setting as these patients may not be representative for all Iranian patients especially in non-public centres. These issues should be considered in interpreting our study.

Conclusions

In summary, the results showed that IEV versus ESHAP was dominant in the treatment of patients with lymphoma in short-term. In terms of incremental cost-effectiveness analysis, ICER was $109749.23 (using IEV saves $109749.23 per each additional effectiveness). Therefore, it is recommended that oncologists should use IEV instead of ESHAP in the treatment of these patients. We suggest that a long-term economic analysis is necessity whenever data is available to knowingly decision making. We hope that this study can bring the interests of policy makers and researchers to conduct economic evaluation studies in healthcare system of Iran.

Acknowledgement

This research was performed by Mr. Mostafa habibian, in partial fulfilment of the requirements for certification as an MSc in Health Economic School at Shiraz University of Medical Sciences in Shiraz, Iran. The present article was adopted from the proposal number 7044 approved by Vice-Chancellor for Research Affairs of Shiraz University of Medical Sciences.

References

1. Kazemzendehdel (2010) Iranian national cancer registration Re-port, 2010 Tehran.
2. Longo DL, Duffey PL, Young RC, Hubbard SM, Ihde DC, et al. (1992) Conventional-dose salvage combination chemotherapy in patients relapsing with Hodgkin's disease after combination chemotherapy: the low probability for cure. J Clin Oncol 10: 210-218.
3. **Schottenfeld D, Fraumeni JF (2006) Director, Cancer Epidemiology and Prevention. 2006: Oxford University Press, USA.**
4. American Cancer Society, Cancer Facts & Figures 2014.
5. Fisher RI, Gaynor ER, Dahlberg S, Oken MM, Grogan TM, et al. (1993) Comparison of a standard regimen (CHOP) with three intensive chemotherapy regimens for advanced non-Hodgkin's lymphoma. N Engl J Med 328: 1002-1006.
6. Oza AM, Ganesan TS, Leahy M, Gregory W, Lim J, et al. (1993) Patterns of survival in patients with Hodgkin's disease: long follow up in a single centre. Ann Oncol 4: 385-392.
7. Zinzani PL, Tani M, Molinari AL, Stefoni V, Zuffa E, et al. (2002) Ifosfamide, epirubicin and etoposide regimen as salvage and mobilizing therapy for relapsed/refractory lymphoma patients. Haematologica 87: 816-821.
8. Engert A, Horning SJ (2010) Hodgkin Lymphoma: A Comprehensive update on diagnostics and clinics. Springer.
9. Choi CW, Paek CW, Seo JH, Kim BS, Shin SW, et al. (2002) ESHAP salvage therapy for relapsed or refractory non-Hodgkin's lymphoma. J Korean Med Sci 17: 621-624.
10. Zinzani PL, Barbieri E, Visani G, Gherlinzoni F, Perini F, et al. (1994) Ifosfamide, epirubicin and etoposide (IEV) therapy in relapsed and refractory high-grade non-Hodgkin's lymphoma and Hodgkin's disease. Haematologica 79: 508-512.
11. Mashhadi M, Rahimi H, Najafi B, Khosravi A (2011) IEV (ifosfamide, epirubicin , VP16) regimen as salvage therapy for early relapsed/refractory Hodgkin and non-Hodgkin's Lymphoma. International Journal of Hematology-oncology and Stem Cell Research 5: 11-15.
12. Wang WS, Chiou TJ, Liu JH, Fan FS, Yen CC, et al. (1999) ESHAP as salvage therapy for refractory non-Hodgkin's lymphoma: Taiwan experience. Jpn J Clin Oncol 29: 33-37.
13. Iranian National Cancer. Iranian national cancer registration report. 2010: Tehran.
14. Mousavi S (2007) Executive Guideline for Registering and Reporting Cancer Cases.
15. Rodriguez MA, Cabanillas FC, Velasquez W, Hagemeister FB, McLaughlin P, et al. (1995) Results of a salvage treatment program for relapsing lymphoma: MINE consolidated with ESHAP. J Clin Oncol 13: 1734-1741.
16. Hackshaw A, Sweetenham J, Knight A (2004) Are prophylactic haematopoietic growth factors of value in the management of patients with aggressive non-Hodgkin's lymphoma? Br J Cancer 90: 1302-1305.
17. Johnston KM, Marra CA, Connors JM, Najafzadeh M, Sehn L et al., (2010) Cost-effectiveness of the addition of rituximab to CHOP chemotherapy in first-line treatment for diffuse large B-cell lymphoma in a population-based observational cohort in British Columbia, Canada. Value Health 13: 703-711.
18. Kuderer NM, Dale DC, Crawford J, Cosler LE, Lyman GH (2006) Mortality, morbidity, and cost associated with febrile neutropenia in adult cancer patients. Cancer 106: 2258-2266.
19. Leese B, Collin R, Clark DJ (1994) The costs of treating febrile neutropenia in patients with malignant blood disorders. Pharmacoeconomics 6: 233-239.
20. Ray JA, Carr E, Lewis G, Marcus R (2010) An evaluation of the cost-effectiveness of rituximab in combination with chemotherapy for the first-line treatment of follicular non-Hodgkin's lymphoma in the UK. Value Health 13: 346-357.
21. Van Agthoven M, Vellenga E, Fibbe WE, Kingma T, Uyl-de Groot CA (2001) Cost analysis and quality of life assessment comparing patients undergoing autologous peripheral blood stem cell transplantation or autologous bone marrow transplantation for refractory or relapsed non-Hodgkin's lymphoma or Hodgkin's disease. a prospective randomised trial. Eur J Cancer 37: 1781-1789.
22. Woronoff-Lemsi MC, Arveux P, Limat S, Deconinck E, Morel P, et al. (1997) Cost comparative study of autologous peripheral blood progenitor cells (PBPC) and bone marrow (ABM) transplantations for non-Hodgkin's lymphoma patients. Bone Marrow Transplant 20: 975-982.
23. Zinzani PL (2002) Ifosfamide, epirubicin and etoposide regimen as salvage and mobilizing therapy for relapsed/refractory lymphoma patients. Haematologica 87: 816-821.