

## SAFETY AND EFFICACY OF THREE TREATMENT REGIMENS OF R-CHOP, E-CHOP, AND R-CHOEP IN NON-HODGKIN LYMPHOMA CANCER PATIENTS

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Received: 19 December 2017, Revised and Accepted: 07 March 2018

### ABSTRACT

**Objective:** This study was designed to investigate safety, efficacy of different regimens such as R-CHOP, E-CHOP, and R-CHOEP used in the treatment of in non-Hodgkin lymphoma (NHL) cancer patients.

**Methods:** Available and required data of 64 NHL cancer patients were collected. Data were related to demography of patients, name of the drug, dose, route, frequency, duration of therapy, and investigational reports.

**Results:** This study showed some variation and similarities in different regimens. Arm-A (R-CHOP) and Arm-B (E-CHOP) showed similar result for Eastern Cooperative Oncology Group (ECOG) score 2 but showed different result of ECOG score 0 and 1. High percentage of patient was taken in Arm-A and Arm-B as compared to Arm-C (R-CHOEP) for ECOG score 2. Surprisingly, it was found that very few percentages of patients showing progressive disease during R-CHOEP as compared to R-CHOP, E-CHOP therapy.

**Conclusion:** From this study, it was concluded that Arm-C (R-CHOEP) showed better result in comparison of Arm-A (R-CHOP) and Arm-B (E-CHOP). As far as toxicity is concern, early detection and personalized management may improve clinical outcome and tolerance.

**Keywords:** Non-hodgkin lymphoma, Eastern Cooperative Oncology Group score, Prognostic index, Response evaluation criteria in solid tumors criteria.

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### INTRODUCTION

Lymphoma is the type cancer where tumors begin in infection-fighting cells of the immune system, called lymphocytes [1]. There are many subtypes of lymphomas [2]. The Hodgkin lymphomas (HLs) and the non-HL (NHLs) comes under major category of lymphoma [3,4]. About 90% of lymphomas are non-HLs [5,6]. NHL does not involve Reed-Sternberg cells. There are more than 61 different types of NHL, some of which are more frequent than others [7]. Autoimmune diseases, HIV/AIDS, infection with human T-lymphotropic virus, immunosuppressant medications increase the risk of NHLs [2]. Eating large amounts of red meat may also increase the risk lymphoma [8-10].

There were about 19.7 cases of NHL per 100,000 adults per year, 6.3 deaths per 100,000 adults per year in the USA [11].

In KSA, NHL accounting for 703 cases and 7.1% of all newly diagnosed cancers in the year 2010. It affected 407 (57.9%) males and 296 (42.1%) females with a male-to-female ratio of 138:100. The median age was 49 years among males (range 0-101 years) and 55 years among females (range 2-92 years) [12].

R-CHOP regimen has been the first-line chemotherapy for NHL patients. CHOP is also prescribed as chemotherapy regimen for NHL in some clinical settings [13]. However, the efficacy and safety of these three regimens (R-CHOP, E-CHOP, and R-CHOEP) have not been head-to-head compared in a randomized study. The aim of this study is to compare the efficacy and safety of R-CHOP, E-CHOP, and R-CHOEP in previously untreated NHL patients.

### METHODS

Research was carried out in compliance with the Helsinki Declaration with completion of certificate (Certificate number: 2086281) from

National Institute of Health office of extramural research protecting human research participants. The consent was about not to disclose the name of patient and data collected from treatment chart, patient's case note, and laboratory investigational reports, and data that will be used only for publication purpose.

### Patient enrolment

Patient was taken (Fig. 1) in consideration for this study on the basis of following inclusion and exclusion criteria.

### Inclusion criteria

- Positive diffuse large B-cell lymphoma
- Histological or cytological confirmed or metastatic carcinoma of NHL
- Ann Arbor stage I-IV
- Eastern Cooperative Oncology Group (ECOG) physical score of 0-2
- Have at least one clinically measurable lesion:  $\geq 2$  cm under physical examination
- Life expectancy of  $\geq 3$  months
- Age between 18 and 70 years
- Patient at least completed two cycles of chemotherapy
- Both sexes (male and female)
- SGOT, SGPT, and total bilirubin  $\leq 2 \times$  upper limit of normal (ULN)
- Glomerular filtration rate (MDRD method)  $\geq 30$  mL/min
- No evidence of HIV and active hepatitis B or C virus
- Cardiac function of Class I-II in New York Heart Association classification.

### Exclusion criteria

- Indolent lymphoma patients
- Serum Epstein-Barr virus DNA  $\geq 1000$  copies/mL
- Double-hit lymphoma confirmed by fluorescence *in situ* hybridization (FISH)
- Primary mediastinal B-cell lymphoma
- Central nervous system problem.

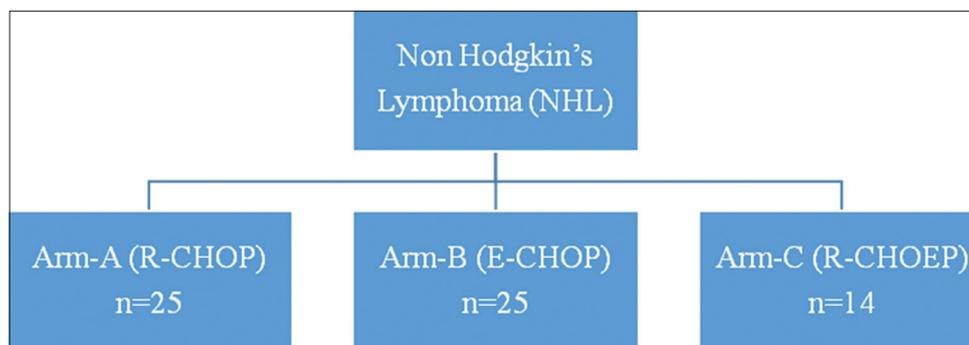


Fig 1: Distribution of different regimen (n is the number of patient)

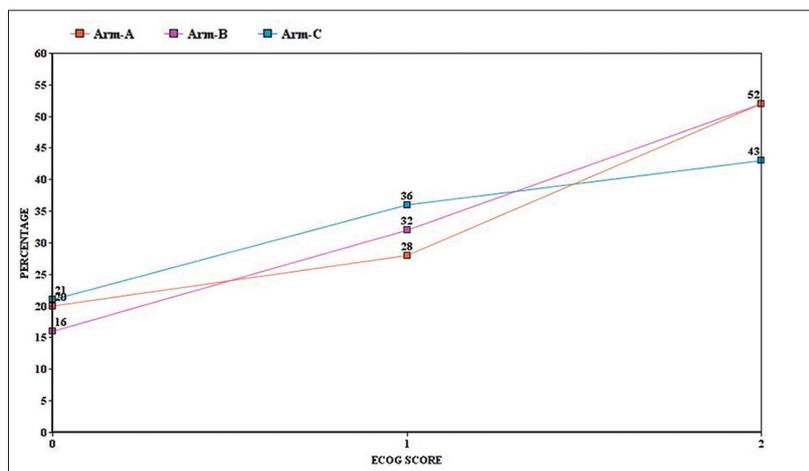


Fig 2: Eastern Cooperative Oncology Group Score among all three regimens

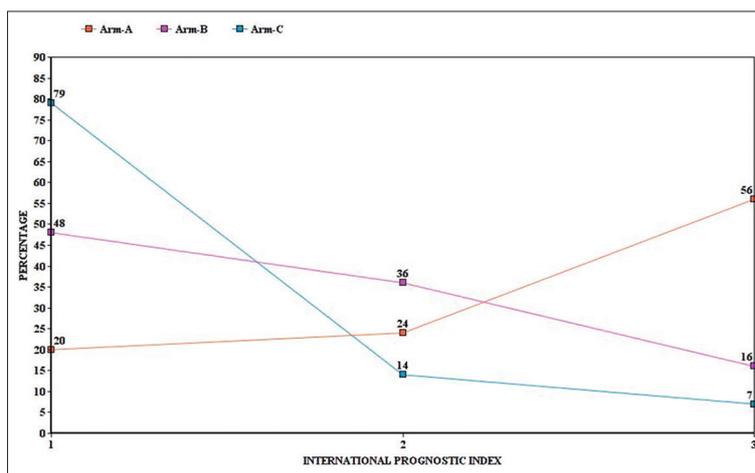


Fig 3: Prognostic index among all three regimens

Table 1: Dosing schedule of R-CHOP regimen

Drug	Dose	Mode	Days
Rituximab	375 mg/m <sup>2</sup>	IV	Day 1
Prednisolone	60 mg/m <sup>2</sup>	PO	Days 1-5
Oncovin	0.4 mg/m <sup>2</sup>	IV	Days 1-4
Cyclophosphamide	750 mg/m <sup>2</sup>	IV	Day 5
Hydroxydaunorubicin	10 mg/m <sup>2</sup>	IV	Days 1-4

**Collection of data**

Available and required data of 64 NHL cancer patients were collected. Data were related to demography of patients, name of the drug, dose,

route, frequency, duration of therapy, and investigational reports. Drug regimens are summarized in Tables 1-3.

**Evaluation of toxicity**

All hematological, non-hematological toxicity were evaluated as per Common Terminology Criteria for Adverse Events v4.0.

**Statistical analysis**

The data were collected to compare the safety, efficacy, and toxicity between Arm-A, Arm-B, and Arm-C. Values were expressed as percentages. Comparison of the mean values within the group was done using t-test. p<0.05 was considered to indicate statistical significance. Statistical analysis was performed by SAS software version 9.4.

**Table 2: Dosing schedule of EPOCH regimen**

Drug	Dose	Mode	Days
Etoposide	50 mg/m <sup>2</sup>	IV	Days 1-4
Prednisolone	60 mg/m <sup>2</sup>	PO	Days 1-5
Oncovin	0.4 mg/m <sup>2</sup>	IV	Days 1-4
Cyclophosphamide	750 mg/m <sup>2</sup>	IV	Day 5
Hydroxydaunorubicin	10 mg/m <sup>2</sup>	IV	Days 1-4

**Table 3: Dosing schedule of R-EPOCH regimen**

Drug	Dose	Mode	Days
Rituximab	375 mg/m <sup>2</sup>	IV	Day 1
Etoposide	50 mg/m <sup>2</sup>	IV	Days 1-4
Prednisolone	60 mg/m <sup>2</sup>	PO	Days 1-5
Oncovin	0.4 mg/m <sup>2</sup>	IV	Days 1-4
Cyclophosphamide	750 mg/m <sup>2</sup>	IV	Day 5
Hydroxydaunorubicin	10 mg/m <sup>2</sup>	IV	Days 1-4

**Table 4: Patient's characteristics of all three regimens NHL patients**

Characteristic	n (%) - Arm-A	n (%) - Arm-B	n (%) - Arm-C
Middle age (range)	43 years old (18-70)	46 years old (18-70)	47 years old (18-70)
Gender			
Male	20 (80)	19 (76)	10 (71)
Female	5 (20)	6 (24)	4 (29)
Clinical staging			
Grade II	11 (44)	10 (40)	6 (43)
Grade IV	14 (56)	15 (60)	8 (57)
ECOG score			
0	5 (20)	4 (16)	3 (21)
1	7 (28)	8 (32)	5 (36)
2	13 (52)	13 (52)	6 (43)
International prognostic index			
0-1	5 (20)	12 (48)	11 (79)
2	6 (24)	9 (36)	2 (14)
3	14 (56)	4 (16)	1 (7)
Others			
Weight lose	15 (60)	13 (52)	5 (36)
Neutropenic fever	20 (80)	10 (40)	6 (43)
Pneumonia	18 (72)	13 (52)	4 (29)
LDH (>240 IU/L)	22 (88)	15 (50)	3 (21)
Efficacy parameter: RECIST criteria			
CR	2 (8)	4 (16)	3 (21)
PR	13 (52)	18 (72)	10 (71)
SD	7 (28)	2 (8)	2 (14)
PD	3 (12)	1 (4)	0 (0)

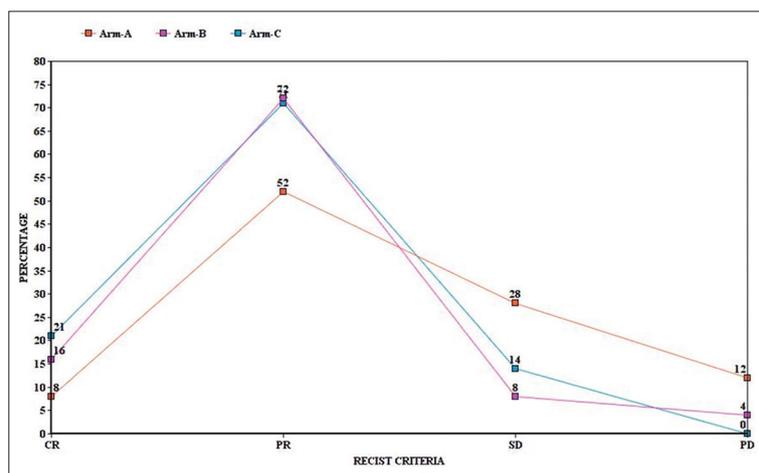
RECIST: Response evaluation criteria in solid tumors, CR: Complete response, PR: Partial response, SD: Stable disease, PD: Progressive disease, ECOG: Eastern Cooperative Oncology Group

**RESULTS**

A total of 64 patients with NHL treated with first-line chemotherapy were identified. Patient was classified in different clinical staging and found in Grade II and IV. Patient showed different ECOG score. Maximum number of patient was showing ECOG score 2. In Arm-A, maximum number of patient showed international prognostic index 3, but Arm-B and Arm-C showed international prognostic index 0-1. Other biological and diagnostical parameters were also taken into account. All the three groups were examined for response evaluation criteria in solid tumors (RECIST) to know the efficacy of different regimen. Patient's characteristics are summarized in Table 4.

**DISCUSSION**

In 1997, rituximab was approved for medical use [14]. According to the WHO, it is the most effective and safe medication for the treatment of lymphoma [15,16]. It is used to treat NHL and predominantly different subtypes of Hodgkin's lymphoma [17]. In the USA, etoposide was



**Fig 4: Response evaluation criteria in solid tumors criteria of all three regimens**

approved in 1983 [18]. Besides that, it is also used before bone marrow or blood stem cell transplant [19].

For this study, similar number of patients was found in Arm-A and Arm-B, but there was less number of patients in Arm-C. This study showed some variation and similarities in different regimen. Arm-A (R-CHOP) and Arm-B (E-CHOP) showed similar result for ECOG score 2 but showed different result of ECOG score 0 and 1. High percentage of patient was taken in Arm-A and Arm-B as compared to Arm-C for ECOG score 2 (Fig. 2).

For prognostic index, high percentage of patients was found in low risk for Arm-C as compared to Arm-B and Arm-A. Similarly, there was low percentage of patients in case of Arm-C as compared to Arm-B and Arm-A (Fig. 3).

Different regimen was compared for RECIST, and it was found comparative result with Arm-C. There was more percentage of patients showing complete response with Arm-C as compared to Arm-A and Arm-B. Surprisingly, it was found that very few percentages of patients showing progressive disease during R-CHOEP as compared to R-CHOP, E-CHOP therapy (Fig. 4).

### CONCLUSION

From this study, it was concluded that Arm-C (R-CHOEP) showing better efficacy as compared to Arm-A (R-CHOP) and Arm-B (E-CHOP). An early detection of toxicity and personalized management may improve clinical outcome and tolerance. However, these results need additional information regarding prognostic factors and patients with advanced NHL should be validated in prospective studies.

### ACKNOWLEDGMENT

We would like to thank Dr. Aysha Almana, Dr. EmadAlbaba, Mrs. Amal Kolghassi, and Dr. Yousif Amin, MACHS, for supporting and making successful completion of this study.

### CONFLICTS OF INTEREST

The authors declare that there are no conflicts of interest.

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