MADRID 2014 ESMO congress

Results of interim analysis of prospective randomized multicenter open-label study in comparison of efficacy and toxicity of BEACOPP-14 and BEACOPP-esc regimens in patients with Hodgkin's lymphoma from poor-prognosis group

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Disclosure

- No conflict of interests

Background

USA, Europe:

Incidence of HL

2.0-3.2 per 100000

5-y-OS 84.0 %;

III-IV stages 76.0 %;

Mortality of HL

0.3-0.5 per 100000

(Surveillance, Epidemiology, and End Results Program, Cancer Research UK)

Ukraine:

Incidence of HL

2.4 per 100000

5-y-OS 63.3 %;

III-IV stages 41.5 %;

Mortality of HL

1.0 per 100000

(National Cancer Register)

Background

ABVD 5-y-OS 66%
(Ukrainian National Cancer Register)

30-40% patients need ASCT after ABVD *(Josting, 2002);*
60 ASCT per year are performed in Ukraine, while
>1000 ASCT per year are needed

First line therapy intensification

BEACOPP-esc 5-y-OS 92% (HD9 study);

BECOPP-14 OS 97% at 34 months (95% CI, 93% to 100) (Sieber, 2003)

Study design

N=215 pts
5 centers
Enrollment 2008-2013

Patients 18-65 years old

Hodgkin's lymphoma

Stage IIB >1 RF, III, IV

ECOG 0-2

Arm A

BEACOPP-esc

n=117

Cyclophosphamide 1250 mg/m^2 d1
Doxorubicin 35 mg/m^2 d1
Etoposide 200 mg/m^2 d1-3
Procarbazine 100 mg/m^2 d1-7
Prednisolone 40 mg/m^2 d1-14
Bleomycin 10 mg/m^2 d8
Vincristine 1.4 mg/m^2 d8

Radiation therapy

PET+, initial sites > 5 cm, residual disease >2 cm

Arm B

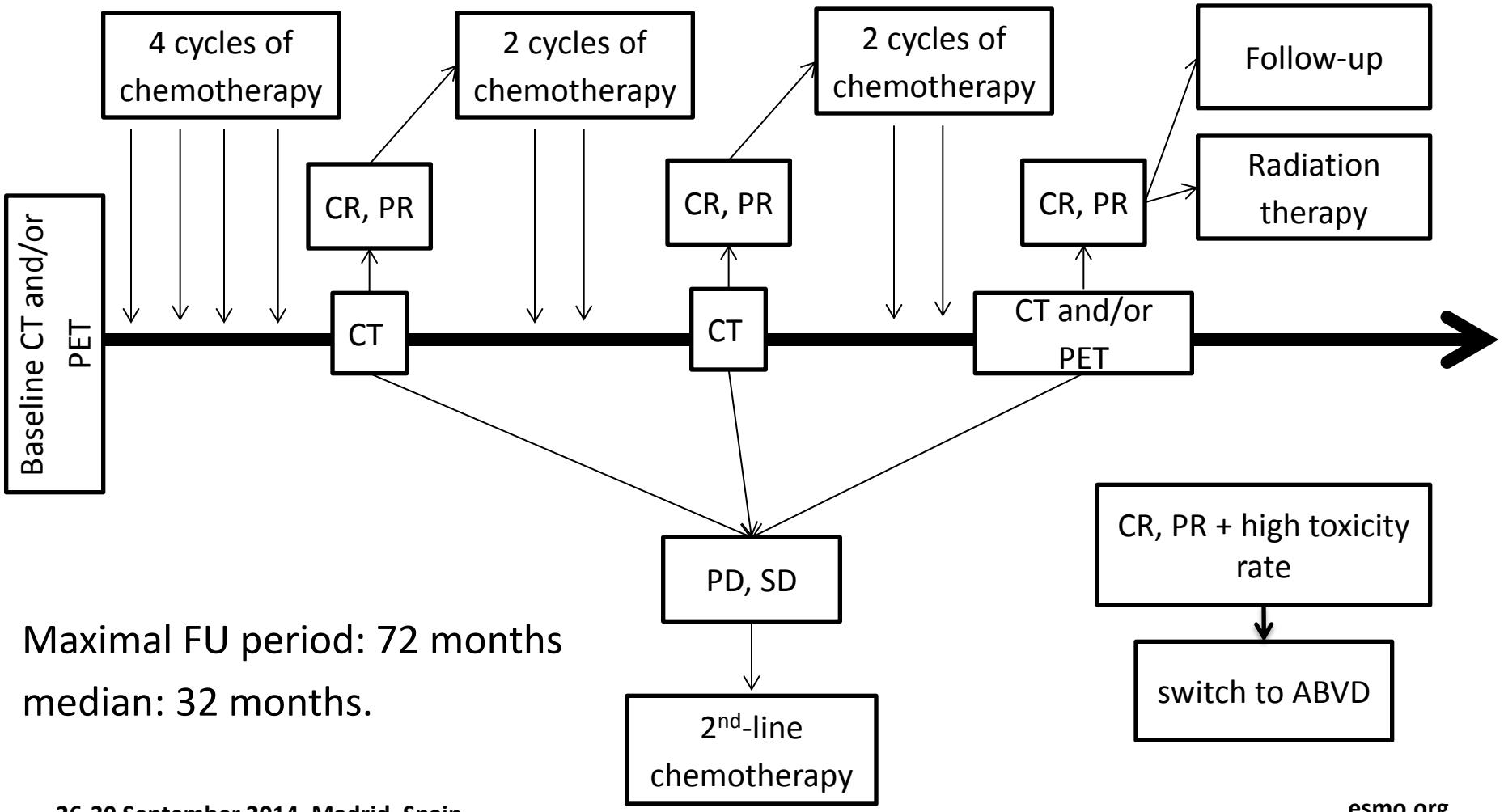
BEACOPP-14

n=98

Cyclophosphamide 650 mg/m^2 d1
Doxorubicin 25 mg/m^2 d1
Etoposide 100 mg/m^2 d1-3
Procarbazine 100 mg/m^2 d1-7
Prednisolone 40 mg/m^2 d1-8
Bleomycin 10 mg/m^2 d8
Vincristine 1.4 mg/m^2 d8

Primary endpoint: 3-year PFS.
Secondary endpoints: ORR, complete response (CR) rate, partial response (PR) rate, 3-year OS and toxicity rate.

Study design



Maximal FU period: 72 months

median: 32 months.

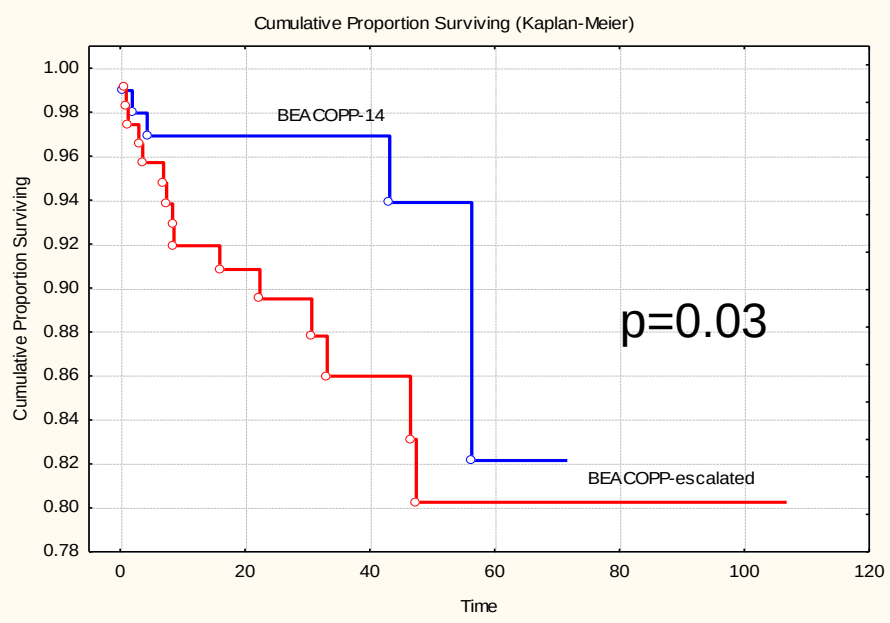
Patients' groups characteristics

Characteristic	BEACOPP-esc	BEACOPP-14	p
No of patients	117	98	
Median of age, years	31	30	>0.05
Gender			
Male, No(%)	56 (48)	34 (35)	>0.05
Female, No(%)	61 (52)	64 (65)	>0.05
Stage			
IIB, No(%)	28 (24)	28 (29)	>0.05
III, No(%)	44 (38)	33 (33)	>0.05
IV, No(%)	45 (38)	37 (38)	>0.05
B-symptoms, No(%)	85 (73)	69 (70)	>0.05
Radiotherapy, No(%)	64 (55)	45 (46)	>0.05
Switch to ABVD	38 (32)	16 (16)	<0.05

Treatment efficacy

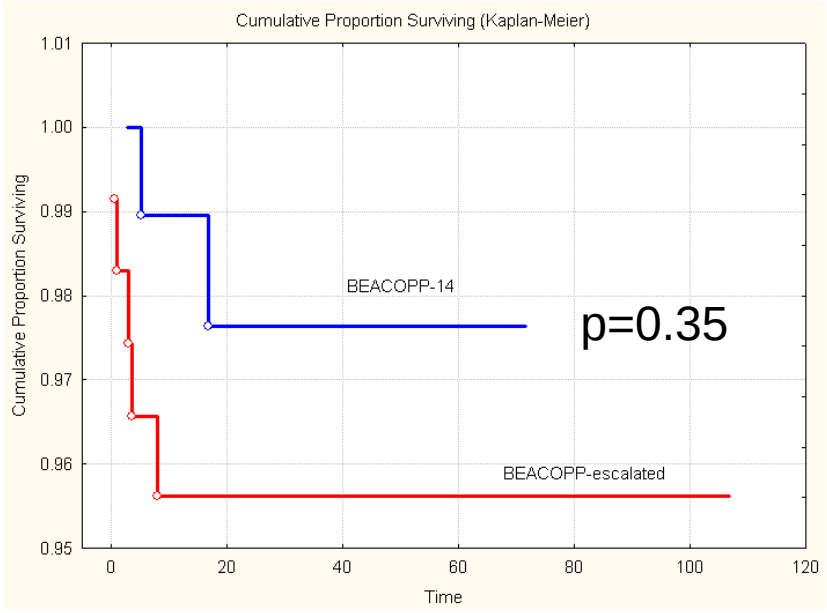
Response and survival	BEACOPP-esc	BEACOPP-14	p
ORR, No(%)	115 (98.3)	96 (98.0)	>0.05
CR, No(%)	86 (73.5)	79 (81)	>0.05
PR, No(%)	29 (24.8)	17 (17)	>0.05
PD, No(%)	2 (2)	2 (2)	>0.05
Relapse, No (%)	10 (9)	4 (4)	>0.05
3-year PFS, %	85.1	93.9	0.03
3-year OS, %	92.6	94.2	0.35
Death rate, No (%)	5 (5)	2 (2)	>0.05
Due to disease progression, No (%) Due to toxicity, No (%)	2 (2) 3 (3)	2 (2) 0 (0)	>0.05 >0.05

3-year PFS



Log-Rank Test WW = -4.143 Sum = 19.805 Var = 4.9355 Test statistic = -1.86467 p = .06223
ariable: month 2
Variable with censoring indicator: cenz2
Grouping variable: group
Total number of valid observations: 215
uncensored: 20 (9.30%) censored: 195 (90.70%)
Valid observations: Group 1 (BEACOPP-): 98 Group 2 (BEACOPP-): 117
Uncensored: 5 (5.10%) 15 (12.82%)
Censored: 93 (94.90%) 102 (87.18%)

3-year OS



Log-Rank Test WW = -1.247 Sum = 6.9649 Var = 1.7357 Test statistic = -.946252 p = .34402
Variable: month
Variable with censoring indicator: cenz 1
Grouping variable: group
Total number of valid observations: 215
uncensored: 7 (3.26%) censored: 208 (96.74%)
Valid observations: Group 1 (BEACOPP-): 98 Group 2 (BEACOPP-): 117
Uncensored: 2 (2.04%) 5 (4.27%)
Censored: 96 (97.96%) 112 (95.73%)

Toxicity rates

Toxicity type	BEACOPP-esc (771 cycles, med 6.5)	BEACOPP-14 (690 cycles, med 6.9)	p
Anemia, No(%)	347 (46)	317 (46)	
grade 3-4, No(%)	107 (14)	111 (16)	
Leukopenia, No(%)	410 (49)	359 (52)	
grade 3-4, No(%)	295 (39)	286 (41)	
Neutropenia, No(%)	352 (47)	357 (52)	
grade 3-4, No(%)	310 (41)	314 (46)	p<0.05
Thrombocytopenia, No(%)	92 (12)	88 (13)	
grade 3-4, No(%)	20 (3)	23 (3)	
Death due toxicity, No(%)	3 (3)	0 (0)	
Alopecia, No(%)	771 (100)	690 (100)	
Mucositis, No(%)	99 (13)	77 (11)	
Febrile neutrop., No(%)	45 (6)	27 (4)	p>0.05
Born children, No	1	6	p>0.05

Conclusions

- BEACOPP-14 and BEACOPP-esc are effective regimens for treatment of Hodgkin's lymphoma in patients from poor prognosis group
- There was no difference in ORR, CRR, and OS at median follow up 32 months (ORR 98.0 % and 98.3 %, CRR 81% and 73.5%, OS was 94.2 % and 92.6 % in BEACOPP-14 and BEACOPP-esc groups, respectively)
- 3-year PFS was 93.9 % and 85.1 % (p=0.03) in BEACOPP-14 and BEACOPP-esc groups
- Both regimens had comparable toxicity rates
- The level of neutropenia gr. 3-4 was significantly higher in BEACOPP-14 group (46% vs 41% in the group of BEACOPP-esc)
- Early intensification could be a good option particularly for those countries where ASCT is not available for all relapsed patients
- The obtained data are promising, but longer follow up is required to confirm these results.

Acknowledgments

- Oleynik V.S.,
  Clinical Hospital №2, Hematology Department, Kharkiv;
- Kiseleva M.Y.,
  Oncologic al Hospital, Hematology Department, Simferopol;
- Stratienko V.V.,
  Oncological Hospital, Hematology Department, Kherson;
- Vilchevska K.V.,
  Institute of Emergency Medicine and Reconstructive Surgery, Hematology Department, Donetsk;
- Pylypenko G.V.,
  Oncological Hospital, Hematology Department, Cherkassy

THANK YOU FOR YOUR ATTENTION!