Clinical Outcome of P-GEMOX (Pegaspargase, Gemcitabine, Oxaliplatin) for the patients with Newly Diagnosed Stage III/IV or Relapsed/Refractory Extranodal Natural Killer/T Cell Lymphoma

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OBJECTIVES:

Extranodal natural killer/T-cell lymphoma (ENKTL) is an aggressive form of non-Hodgkin's lymphoma.The prognosis for patients with advanced stages or relapsed/ refractory ENKTL is extremely poor[1-5]. Optimal combined chemotherapy remain to be defined [6]. Therefore, the purpose of this study is to evaluate efficacy and safety of P-GEMOX (Pegaspargase, Gemcitabine and Oxaliplatin) in patients with newly diagnosed stage III/IV or relapsed/refractory ENKTL.

METHODS:

We retrospectively analyzed the effectiveness and toxicity of P-GEMOX in 60 patients with newly diagnosed stage III/IV and relapsed/refractory ENKTL between February 2008 and August 2014. The P-GEMOX dosage was as follows: Gemcitabine 1000 mg/m^2 iv d1,d8; Oxaliplatin 100 mg/m^2; d 1, Pegaspargase 2000 U/m^2 im, two different sites. The regimen was repeated every three weeks for a maximum six cycles. Patients underwent autologous hematopoietic stem cell transplantation (ASCT) as consolidation if they achieved CR.

RESULTS:

Fig1. 4-year OS and PFS

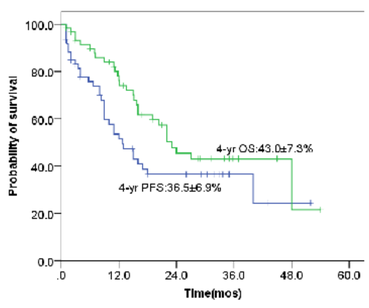


Fig3. OS: ASCT vs. Non-ASCT

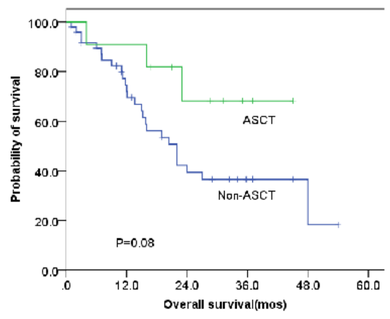
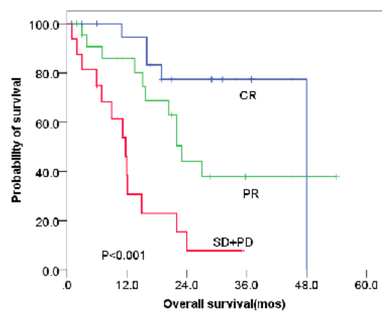


Fig2. Survival, based on response



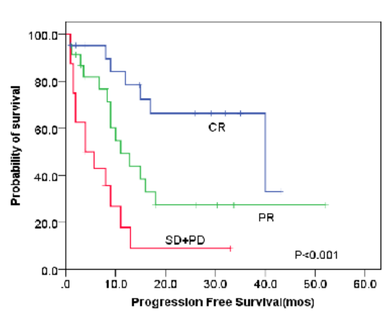


Table 1. Clinical Characteristics

	% (N)
Gender	
Male	73.3 (44)
Female	26.7 (16)
Newly diagnosed	25.0 (15)
Refractory	43.3(26)
Relapsed	21.7(19)
Age	
<60 years	91.7(55)
≥60 years	8.3(5)
PS, ECOG	
0-1	73.3(44)
2	26.7(16)
EBV-DNA level	
Normal	41.7(25)
Elevated	58.3(35)
LDH	
Normal	58.3(35)
Elevated	41.7(25)

	% (N)
Stage, baseline	
I_E	15.0(9)
II_E	16.7(10)
III_E	35.0(21)
IV_E	33.3 (20)
KPI score	
0-1	28.3(17)
2	21.7(13)
3	38.3(23)
4	11.7(7)
IPI score	
0-1	48.3(29)
2	31.7(19)
3-4	20.0(12)
Fever	
Present	46.7(28)
Absent	53.3(32)
Previous No. of CT regimens	8.3(5)
< 2	53.3 (32)
≥ 2	21.7(13)

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1. Between February 2008 and August 2014, 60 consecutive patients were enrolled in this study. 57 patients were available for evaluation of response.

2. The objective response, complete remission(CR), of whole cohort were 73.7% (42/57), 36.8% (21/57), respectively. It can be easily administered in out-patients clinic.

3. The median follow-up was 29.1 (range, 2.4–54.2 months). Median OS and PFS was 23.0 months (95% confidence interval [CI], 16.441-29.559) and 12.8 months(95% confidence interval [CI], 8.109-17.491), respectively. The 4-year OS and PFS rate was 43.0±7.3% and 36.5±6.9%, respectively (Figure1).

4. There was no difference between newly diagnosed stage III/IV and relapsed/refractory in OS and PFS. The long term survival CR responders were superior to patients with other response, and there was significant difference between the three group(Figure 2, P<0.001). Eleven patients accepted ASCT after achievement of CR, 3-year OS rate were better than other patients(68.2% vs. 36.6% , P=0.08, Figure 3).

5. Toxicities (>50%) : neutropenia (85.0%), thrombocytopenia (72.0%), hypoproteinemia (86.7%), and anorexia (63.3%). In addition, hypofibrinogenemia was 46.7%. The most common grade III/IV toxicities (>10%) were granulocytosis (31.6%), thrombocytopenia (26.67%) and hypoproteinemia (13.3%). Intracranial bleeding occurred in one patient during the first cycle with discontinuation of pegaspargase in the consecutive cycles.

6. No treatment related death confirmed.

CONCLUSIONS:

The P-GEMOX regimen is a safe and effective combination for newly diagnosed advanced and relapsed/refractory ENKTL. Promising long term outcome can be expected by addition of ASCT consolidation after response to induction chemotherapy. In comparison to other combined regimen in literatures, P-GEMOX is effective with less toxic, simplified and high cost-effective . Further clinical trials urgently needed .

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T-cell lymphoma

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