

## rhGM-CSF

=Abstract=

### A Clinical Study on the Effect and Toxicity of rhGM-CSF

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Dosage reinforcement of chemotherapeutic agent is thought to be a solution in treating many malignancies, including ovarian cancer and cervical cancer.

The remission rate after administration of chemotherapeutic agents has a positive correlation with dosage and in cases where limitations were put on dosage, improved survival rate was achieved with dose-intensive therapy facilitated by autologous bone marrow transplantation(BMT) or the use of cytokines such as G-CSF.

Our objectives are to evaluate therapeutic efficacy and toxicity of GM-CSF and to elucidate the effect of premedication which was administered to minimize the toxicity of the GM-CSF.

Total number of patients entered into this study was fifty two and they are consisted of thirty seven patients of the uterine cervix, fourteen patients of ovarian cancer and one endometrial cancer patient.

The increase in neutrophil count and WBC count was found to be statistically valid, but the changes in the number of platelets, hemoglobin, neutrophil and monocytes were not shown to be meaningful when statistics are brought in. Administration of GM-CSF resulted in mild toxicities such as myalgia, fever, skin reaction and neuropathy. But, one patient had grade 3 myalgia. Premedication brought about meaningful reductions in the toxicities of GM-CSF and can be used safely to reduce the toxicities.

Keywords: RhGM-CSF, Therapeutic efficacy, Toxicity, Premedication

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(dose intensive chemotherapy) , 4,000 / $\mu\ell$  , 2,000 / $\mu\ell$   
가 가 , 100,000 / $\mu\ell$  , 1.5  
mg/d $\ell$  , SGOT SGPT가 2  
, 1.5 mg/d $\ell$  ,  
50 ml/min  
rhGM-CSF 가  
가 rhGM-CSF 가  
rhGM-CSF 가 가  
(recombinant human granulocyte macrophage colony stimulating factor) (hematopoietic progenitor cell)  
2. 가 4,000/  
 $\mu\ell$  가 2,000/ $\mu\ell$   
rhGM-CSF 250  $\mu\text{g/kg/day}$  7  
가 10,000 / $\mu\ell$   
가  
(colony stimulating factor, CSF) GM-CSF(granulocyte-macrophage stimulating factor)  
2 , 1  
X  
1) AIDS,  
1  
.23) , 2 3  
rhGM-CSF 1 rhGM-CSF 6  
dexamethasone 20mg 30 di-  
phenhydramine 50mg acetaminophen 300  
mg rhGM-CSF 30 6  
2 rhGM-CSF 30 de-  
xamethasone 10 mg 30 pheny-  
ramine maleate 45mg acetaminophen  
600 mg 30 6  
1.  
1996 5 1997 4  
, 4  
, ECOG  
가 0 2, 10 g/d $\ell$  가 1 가 37 , 가 14 ,  
가 52

platinum  
6 platinum  
8 paclitaxel  
rhGM-CSF  
가 3432 + 2024, 1243 + 774  
11762 + 4373, 4961 + 1913  
가 (p < 0.01),  
가 (Table 1).  
1313 + 1351,  
246 + 413 5267 + 2654, 1864 + 1264  
가 (p < 0.01)(Table 2).

Table 1. Effects of administration of rhGM- CSF on hematologic changes

	before	after	p-value
hemoglobin(g/dl)	10.6 ± 3.5	9.2 ± 2.8	0.043
platelet(× 103/ $\mu$ l)	252 ± 120	310 ± 179	0.081
WBC(/ $\mu$ l)	3432 ± 3116	11762 ± 4373	< 0.01
neutrophil	1243 ± 1193	4961 ± 1913	< 0.01
monocyte	422 ± 309	510 ± 356	0.226
eosinophil	169 ± 98	203 ± 112	0.139

Table 2. Effects of administration of rcGM- CSF on bone marrow function

	before	after	p-value
nadir count of WBC	1313 ± 1351	5267 ± 2654	< 0.01
nadir count of neutrophil	246 ± 413	1864 ± 1264	< 0.01

가  
가  
, 1  
(p < 0.01), 1  
가 가  
(Table 3, 4).  
rhGM-CSF 14  
8 (57%) 3

1 2  
(14%) 가 (36%), (29%),  
(Table 5).  
rhGM-CSF 6  
dexamethasone 20 mg , 30 diphenhy-  
dramine 50 mg , 30 6 aceta-  
minophen 300mg 1  
17 4 (24%)  
1 (Table 6).  
rhGM-CSF 30  
dexamethasone 10mg , phenyramine maleate 45mg  
, 30 6 acetaminophene 600mg  
2 21 3  
(14%) 2  
1  
(Table 7).

Table 3. Effects of administration of rhGM- CSF on WBC count according to premedication

	before	after	p-value
control(n = 14)	3037 ± 1666	8012 ± 3135	< 0.01
premed-1(n = 17)	4342 ± 3420	16850 ± 5415	< 0.01
premed-2(n = 2)	2761 ± 1510	10125 ± 4392	< 0.01

Table 4. Effects of rcGM- CSF on neutrophil count according to premedication

	before	after	p-value
control(n = 14)	1168 ± 412	3365 ± 1410	< 0.01
premed-1(n = 17)	1961 ± 1332	6908 ± 2274	< 0.01
premed-2(n = 21)	1020 ± 543	4455 ± 1976	< 0.01

Table 5. Toxicities encountered in the control group(n = 14)

	G1	G2	G3	G4	Total
fever	3	1	0	0	4(29%)
myalgia	3	1	1	0	5(36%)
skin reaction	2	1	0	0	3(21%)
central neuropathy	1	1	0	0	2(14%)
peripheral neuropathy	1	0	0	0	1(7%)
nausea/vomiting	1	1	0	0	2(14%)
cardiac symptom	1	0	0	0	1(7%)
pulmonary symptom	1	0	0	0	1(7%)
total No. of patients	5	3	1	0	8(57%)
total No. of complications	13	5	1	0	19

Table 6. Toxicities encountered in the premedicated group- 1(n = 17)

	G1	G2	G3	G4	Total
fever	2	0	0	0	2(12%)
myalgia	1	0	0	0	1(6%)
skin reaction	1	0	0	0	1(6%)
nausea/vomiting	1	0	0	0	1(6%)
total No. of patients	4	0	0	0	4(24%)
total No. of complications	5	0	0	0	5

Table 7. Toxicities encountered in the premedicated group- 2(n = 21)

	G1	G2	G3	G4	Total
fever	2	0	0	0	2(10%)
pulmonary symptom	0	1	0	0	1(5%)
nausea/vomiting	1	0	0	0	1(5%)
total No. of patients	2	1	0	0	3(14%)
total No. of complications	3	1	0	0	4

CSF) glycoprotein , growth factor gene cloning .67) GM-CSF(gra-  
 cytokine .45) (colony stimulating factor; rhGM-CSF E.coli GM-CSF 1 × 10<sup>8</sup> units  
 nulocyte-macrophage colony stimulating factor) Ga- ssone 8 (1984) Wong6) cloning mammalian cell  
 .45) (colony stimulating factor; rhGM-CSF E.coli GM-CSF 1 × 10<sup>8</sup> units  
 /mg protein 가 , yeast GM-CSF 4 - 5 × 10<sup>7</sup>  
 units/mg protein 가 , Cos cell GM-CSF 8 ×  
 10<sup>6</sup> units/mg protein 가 G-CSF(granulocyte colony stimulating

1

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GM-CSF

23).

,16) GM-CSF

GM-CSF

1

14%

가

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52 rhGM-CSF

1) rhGM-CSF , 가 (p < 0.01)

2) rhGM-CSF 57% 2 (29%), 3 (36%), (14%)

3) 1 2 rhGM-CSF rhGM-CSF (compliance)

가 rhGM-CSF

rhGM-CSF rhGM-CSF

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