Chapter 4

RESULTS

Baseline Characteristics

Total 35 patients were accrued since June 1995 through January 1997. Five patients, 3 in low-dose arm and 2 in conventional-dose arm, were lost to follow up before 4 weeks and 2 patients, one in each arm, were found ineligible by concomitant steroids use during study. There were 14 patients who complete 4 weeks duration of study left balanced in each arms. Selected patient characteristics and underlying malignancy are shown in Table 1. Patient characteristics were similar at baseline for all variables.

At the end of study 12 patients were died from cancer related causes. Others could not be stated due to loss to follow up. One patient in each arm was unable to respond to quality of life questionnaire due to communication obstacle. No patient withdrew from study because of toxicity or excessive weight gain.

Table 1. Patient Characteristics At Baseline In The Two Treatment Groups

Characteristics	Low Dose MA	Conventional MA	Statistics	p Value
Number	14	14	-	-
Male:Female	8:6	10:4	Chi-square	0.43
Mean age $\pm$ SD	56.7 (10.3)	57.5 (13.5)	t-test	0.86
Performance Status				
1	11	9	Chi-square	0.40
2	3	5		
Serum Albumin (g/dl)	3.7	3.9	t-test	0.55
Hemoglobin (g/dl)	10.5	12.7	t-test	0.04
Primary Organ				
Lung	8	9	-	-
Liver	3	2	-	-
Others	3	3		
Concurrent Treatment	8	7	Chi-square	0.70
Chemotherapy	6	5	-	-
Radiation	2	2	-	-
Prestudy Weight Loss (kg)	13.7 (7.2)	14.2 (5.9)	t-test	0.83
Baseline BMI (kg/m^2)	23.3 (3.7)	22.9 (3.9)	t-test	0.77

*Values are mean (SD) where appropriate.

Body Weight and Body Mass Index

Mean body weight change from baseline at week 4 was similarly decreased in both groups (Table 2). Mean percent of body weight change compared with baseline was also decreased in both groups. However, there was a difference in the number of patients who gained weight between two arms. The conventional dose arm had more number of patients who gained weight, 35.7% versus 21.4%. This figure of difference was not statistically significant by Chi-square test (p=0.40). The body mass index change gave the parallel results with the body weight data.

Table 2. Body Weight and Body Mass Index Change

Variable	Low Dose MA	Conventional MA	Statistics*	p Value
Mean Baseline BW	50.09 [45.9,54.2]	53.57 [44.9,62.2]	t = -0.78	0.44
Week 4 BW	48.80 [44.7,52.8]	52.09 [44.4,59.7]	t = -0.82	0.42
Mean Weight Change	-1.29 [-2.7,0.2]	-1.48 [-3.4,0.4]	t = 0.17	0.86
Mean % Weight Change	-2.48 [-5.2,0.3]	-1.98 [-4.9,0.9]	t = -0.27	0.79
Number Patients Gaining Weight	3/14 (21.4%)	5/14 (35.7%)	Cs = 0.70	0.40
Mean Baseline BMI	19.95 (2.5)	19.64 (3.8)	t = 0.25	0.80
Week 4 BMI	19.44 (2.5)	19.14 (3.2)	t = 0.28	0.78
Mean BMI Change	-0.51 (1.0)	-0.50 (3.2)	t = -0.01	0.99
Mean % BMI Change	-2.48 [-5.2,0.3]	-1.98 [-4.9,0.9]	t = -0.27	0.79

*Cs = Chi-square. Value are mean [95% CI] or (SD) where appropriate.

Considering the effect of concurrent treatment either chemotherapy or radiotherapy, mean of percent weight change and percent BMI change were also decreased in both study groups. The effect of treatment was borderline statistical significance concerning the difference of number of patients with weight gain between group with and without concomitant treatment by Chi-square test with p = 0.06 (Table 3).

Table 3. Effect of Concurrent Treatment on Body Weight and Body Mass Index

Variable	Treatment	No Treatment	Statistics*	p Value
Mean % Weight Change	-3.32 [-3.7, -1.8]	-0.98 [-6.0,-0.5]	t = 1.29	0.21
Mean % BMI Change	-3.32 [-3.7, -1.8]	-0.98 [-6.0,-0.5]	t = 1.29	0.21
Number Patients Gaining Weight	2/15 (13.3%)	6/13 (46.2%)	Cs = 3.67	0.06

*Cs = Chi-square. Value are mean [95% CI] where appropriate.

Anthropometric Measurement

All of anthropometric measurement changes were decreased along with the body weight change (Table 4). Tricep skinfold which is reflected body fat mass was more decreased in the conventional dose group than the low dose group. The amount of muscle loss in 40 mg/d MA was more than 160 mg/d MA group without statistical significance. On the contrary, mid-arm fat area was more decreased in conventional megestrol acetate group.

Table 4. Anthropometric Measurement Data Between Both Groups

Variable	Low Dose MA	Conventional MA	t	p Value
Mean Baseline MAC	255.2 (33.1)	243.3 (40.9)	0.85	0.41
Mean Week 4 MAC	246.4 (20.9)	238.7 (35.8)	0.70	0.49
Mean % MAC Change	-2.9 (4.9)	-1.5 (3.9)	-0.86	0.40
Mean Baseline TSF	10.4 (5.0)	12.7 (7.4)	-0.96	0.35
Mean Week 4 TSF	10.7 (5.2)	12.0 (6.9)	-0.59	0.56
Mean % TSF Change	2.3 (18.3)	-3.1 (10.2)	0.96	0.35
Mean Baseline MAMC	22.2 (3.6)	20.3 (2.7)	1.58	0.13
Mean Week 4 MAMC	21.3 (2.4)	20.1 (2.2)	1.40	0.17
Mean % MAMC Change	-3.64 (6.1)	-0.83 (4.3)	-1.41	0.17
Mean Baseline MAMA	4035.8 (1496.9)	3347.6 (884.6)	1.48	0.15
Mean Week 4 MAMA	3651.7 (835.1)	3249.1 (688.4)	1.39	0.18
Mean % MAMA Change	-6.81 (11.2)	-1.48 (8.7)	-1.40	0.17
Mean Baseline MAFA	1230.2 (553.2)	1488.8 (959.4)	-0.87	0.39
Mean Week 4 MAFA	1215.6 (564.8)	1382.5 (870.4)	-0.60	0.55
Mean % MAFA Change	-1.25 (16.9)	-4.09 (12.3)	-0.51	0.62

* Value are mean (SD) where appropriate.

Quality of Life and Appetite Assessment

The difference of general quality of life score between baseline and at week 4 was more improved in the 160 mg/d MA arm than the 40 mg/d MA arm. There were considerable score improvements in the conventional dose arm in physical, family, emotional, and appetite aspects of assessment by questionnaire. Regarding the doctor relationship and working status, there were no obvious difference between the 2 treatment groups (Table 5). However, all of these changes did not reach statistical significance. In appetite evaluation, there was increased mean of score changed regardless of megestrol acetate dose. When considering concurrent treatment effect, similar trend of changes were also shown (Table 6). Interestingly, the group which did not receive chemotherapy or radiation was significantly better in emotional score change.

Table 5. Quality of Life and Appetite Assessment Between Both Groups

Assessment Aspect	Low Dose MA	Conventional MA	t	p Value
QOL at baseline	42.8 (8.3)	44.0 (10.5)		
QOL at week 4	43.2 (9.8)	46.6 (9.8)		
QOL change	0.3 [-3.9,4.5]	2.6 [-3.1,8.3]	-0.71	0.48
Physical	-0.6 [-2.8,1.6]	1.54 [-0.8,3.9]	-1.45	0.16
Family	0.38 [-1.2,1.9]	1.15 [-1.0,3.3]	-0.62	0.54
Emotional	-0.62 [-2.6,1.4]	0.69 [-0.7,2.1]	-1.17	0.26
Doctor Relationship	0.23 [-0.7,1.1]	0.0 [-0.6,0.6]	0.48	0.64
Working	0.38 [-1.8,2.6]	0.54 [-2.1,3.2]	-0.10	0.92
Appetite	2.31 [-4.5,9.0]	3.92 [-2.6,10.4]	-0.38	0.71

* Value are mean [95% CI] where appropriate.

Table 6. Effect of Concurrent Treatment on Quality of Life and Appetite

Assessment Aspect	Treatment	No Treatment	t	p Value
QOL at Baseline	42.1 (8.8)	45.2 (10.1)		
QOL at Week 4	41.9 (8.9)	48.9 (9.7)		
QOL Change	-0.2 [-2.9,2.6]	3.7 [-3.7,11.2]	1.22	0.23
Physical	-0.07 [-2.4,2.2]	1.18 [-1.1,3.5]	0.81	0.43
Family	0.73 [-0.8,2.2]	0.82 [-1.7,3.3]	0.07	0.95
Emotional	-0.93 [-2.3,0.4]	1.36 [-0.6,3.7]	2.15	0.04
Doctor Relationship	0.13 [-0.3,0.6]	0.09 [-1.0,1.2]	-0.09	0.93
Working	-0.13 [1.8,1.5]	1.27 [-2.1,4.6]	0.89	0.38
Appetite	2.07 [-3.0,12.1]	4.55 [-3.8,7.9]	0.57	0.57

* Value are mean [95% CI] where appropriate.

Performance Status

Objective evaluation of patient's physical status was measured by performance status assessment. After 4 week duration of study, the 160 mg/d MA arm had a slight better performance status, compared to baseline, than the 40 mg/d MA arm. While in the concurrent treatment group had slightly higher values of performance status score which indicated a worsening change (Table 7).

Table 7. Performance Status Evaluation

Performance Status	40 mg/d MA	160 mg/d MA	Concurrent Treatment	No Concurrent Treatment
Baseline	1.2 (0.4)	1.3 (0.5)	1.2 (0.4)	1.3 (0.5)
At Week 4	1.3 (0.5)	1.2 (0.4)	1.4 (0.5)	1.2 (0.4)
Difference	0.2 [0.0,0.5]	-0.1 [-0.4,0.3]	0.2 [-0.1,0.5]	-0.1 [-0.5,0.2]

* Value are mean [95% CI] or (SD) where appropriate.

Toxicities

In present study, toxicities were rarely found. Only one patient experienced transient minor vaginal bleeding and needed no treatment. No any episode of edema was detected. The highest weight gain was 5 kg in 4 weeks which was found in one patient in the 160 mg/d MA arm.

Survival Analysis

At the end of study there were 4 patients in low dose arm and 8 patients in conventional dose arm who deceased. Median survival of low dose arm was 22.5 ± 4.9 weeks and 24.4 ±15.1 weeks in conventional dose arm. The log rank test for the difference in survival was not statistically significant with p = 0.16 (figure 1).

Figure 1 Survival Curve by Kaplan-Meier Method