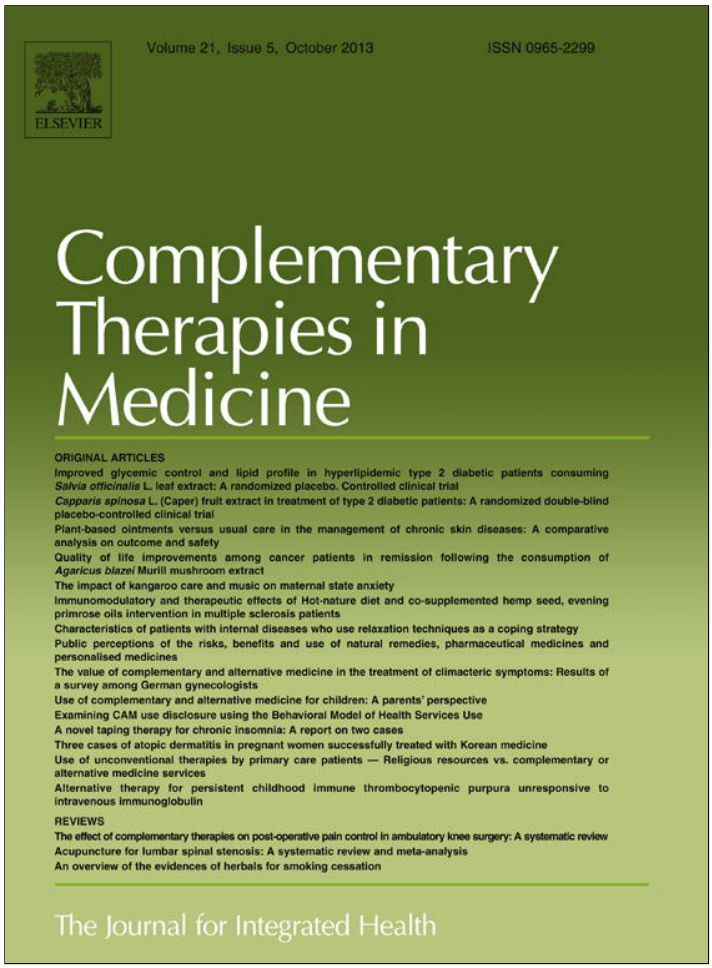

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Quality of life improvements among cancer patients in remission following the consumption of *Agaricus blazei* Murill mushroom extract

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KEYWORDS
Agaricus blazei Murill;
QOL;
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Cancer survivor;
Clinical trial

Summary
Objectives: The aim of this preliminary clinical study was to assess if the daily intake of *Agaricus blazei* Murill (ABM) granulated powder (SSI Co., Ltd., Tokyo, Japan) for 6 months improved the quality of life (QOL) in cancer patients in remission.
Design: Open study.
Setting: Subjects diurnally took 1 (1.8 g; $N = 23$), 2 (3.6 g; $N = 22$), or 3 (5.4 g; $N = 22$) packs/day orally for 6 months.
Main outcome measures: The SF-8 Health Survey questionnaire was used to evaluate the QOL. The differences between the SF-8 baseline scores at the time of entry and 6-months after ABM treatment were evaluated.
Results: The results showed a significant improvement in QOL in both physical and mental components. More specifically, QOL effects of ABM in different genders showed males improved physical components, while females improved only mental components. QOL effects in the different age groups showed that ages 65 and under improved mental components, while ages 66 and older improved physical components. Furthermore, with respect to optimal dose effects of ABM with respect to QOL improvement, two packs per day for 6 months showed improvements in both physical and mental components.
Conclusion: This preliminary longitudinal clinical study demonstrated that daily intake of ABM appears to improve both physical and mental components based on SF-8 qualimetric analysis.

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Introduction

During the past few decades, conventional modalities of cancer therapies included the use of a variety of anticancer drugs, radiation, and surgery targeted at tumors. The resulting severe side effects have compromised the quality of life during and after treatment.[1] In search of a remedy to answer this problem in 1994 the US congress enacted the ''Dietary Supplement Health Education Act.[2] Consequently the use of complementary and alternative medicine (CAM) has proliferated worldwide in order to augment conventional cancer therapies, as well as alleviate and reduce treatment related symptoms and other side effects significantly diminishing the health-related quality of life (HR-QOL).[3–5]

In Japan, the Cancer Research Division, Ministry of Health, Labor and Welfare, has performed a nationwide cross-sectional survey to evaluate the prevalence of CAM use among cancer patients and their perceptions of CAM and specific CAM products.[6] The survey found a prevalence of CAM use, 44.6% (1382 of 3100) among cancer patients in Japan. The most frequently used CAM products among cancer patients were those containing a mushroom, known as *Agaricus blazei* Murill (ABM) (60.6%), popularly known in Japan as ''*Himematsutake*''.

The ABM mushroom is a native to Brazil and widely cultivated in Japan for medicinal purposes. In Japan and elsewhere, ABM is traditionally used to combat a variety of diseases such as cancer,[7–11] diabetes,[12,13] hepatitis, [14,15] hypercholesterolemia,[16] and more recently, radiation toxicity.[17–19] It has been also reported to have antioxidant,[20,21] antimutagenic, [22–24] antiangiogenic,[7,25] antitumorigenic,[8–10,25] apoptotic, [26–29] chemopreventive [30,31] and immuno-stimulative effects.[32–38] Increased lifespan has also been attributable to their use.[39] In addition, ABM has demonstrated clinically that it is an anti-diabetogenic in type II diabetes[13] and that it improves the quality of life in cancer patients undergoing a combination of chemotherapies in gynecological cancer patients.[38] These findings are further supported by the retrospective HR-QOL studies among variety of cancer patients.[40]

The ABM product chosen for this clinical study was Sen-Sei-Ro Powder Gold™ (SSI Co., Ltd., Tokyo, Japan). The rationale for choosing this specific product was based on carefully taking into account both the comprehensive safety study data and the annual consumption numbers. Sen-Sei-Ro is the only ABM product in Japan to complete the 2-year chronic carcinogenic bioassay[39], tripartite genetic, reproductive, neurologic and immunologic toxicities in compliance with the US, FDA guidelines. Furthermore, two previously published clinical studies had also used Sen-Sei-Ro products.[38,40] In addition, annually 70% of Japanese consumers choose Sen-Sei-Ro over that of any other commercial ABM products (from approximately 20 different manufacturers).

Despite the current 20 ton plus annual consumption of ABM-derived CAM products there have not been many clinical studies. This paucity of clinical data prompted the Japanese Ministry of Health, Labor and Welfare to support this clinical study. Albeit, a very limited fund, the present clinical study was undertaken to evaluate quality of life in cancer patients in remission before- and after daily consumption of Sen-Sei-Ro for 6 months.[41]

Table 1 Inclusion criteria for eligibility.

Radical operation for cancer and completely recovered from operation
No cancer therapy within 30 days
No use of supplements
No severe organ dysfunction
Age 20—80
Written informed consent

For the present study, Sen-Sei-Ro was purchased by Public Research Fund, Grant-in-Aid for cancer Research from the Ministry of Health, Labor, and Welfare, Japan. No researcher in this study had any financial or other conflict of interests.

Subjects and methods

This study was approved by the institutional review board of the Kanazawa University Hospital, and Shikoku Cancer Center. Patients were recruited by the Department of Obstetrics and Gynecology of Kanazawa University Hospital and the Department of Urology of Shikoku Cancer Center, respectively. Prior to enrollment, all patients were provided and required to sign written informed consent. Data management with respect to HR-QOL effects of the test supplement was performed independently by the Monitoring and Evaluation Committee for HR-QOL study.

Criteria for the eligibility

Eligibility criteria (Table 1) for inclusion were cancer patients, who were in complete remission with no clinical evidence of relapse of cancer based on (i) a routine follow up clinical evaluation following radical surgery, radiation and chemotherapy; (ii) no cancer therapy within 30 days of onset of the study; (iii) no use of dietary supplements; and (iv) no evidence of severe organ dysfunction (aspartate aminotransferase, alanine aminotransferase, alkaline phosphatase, and γ-glutamyl transpeptidase levels within the upper limits of normal ranges). Patients who met eligibility criteria for the study were recruited between February and August of 2008.

Study protocol

For the purpose of clinical evaluation of HR-QOL effects of Sen-Sei-Ro, a double blind placebo-controlled study design is most ideal, however, due to the limited funding, recruitment of cancer patients was limited to 81 and a longitudinal design was used to defray the available research funding. Three patients out of the initial 81, however, withdrew their consent. The remaining 78 patients were all chosen to be treated with the test product, Sen-Sei-Ro containing 1800 mg of lyophilized, granulated powder per pack. One pack contains the following: carbohydrates 820 mg, protein 488 mg, food grade cellulose (dietary fiber) 284 mg, fat 47 mg and sodium 0.19 mg. According to the 2011 Physician's Desk Reference, water (at 68 mg/pack) contains the following: 0.1 mg Fe, 0.24 mg Ca, 37 mg K, 0.01 mg thiamine, 0.04 mg ergosterol and 0.59 mg niacin. Results from

tests for heavy metals (mercury, cadmium, lead and arsenic) conforms to strict Japanese food regulations. The first 30 subjects were assigned to the lowest dose group (1 pack a day), the next 24 subjects were assigned to the mid-dose group (2 packs/day) and the last 24 subjects were assigned to the highest dose group (3 packs/day). Subjects diurnally took 1 (1.8 g), 2 (3.6 g), or 3 (5.4 g) packs/day orally for 6 months.

HR-QOL assessment

Among the validated instruments to assess quality of life improvement, the SF-8 quality instrument is the simplest form of HR-QOL assessment that has been translated into 30 different languages and used in many countries. In Japan, the SF-8 Health Survey instrument has been critically tested and validated using a standard criteria based on a national survey of 1000 Japanese subjects in 2002.[42] The SF-8 instrument uses 8 short psychometric parameters: (1) general health (GH); (2) physical function (PF); (3) Role physical (RP); (4) bodily pain (BP); (5) vitality (V); (6) social functioning (SF); (7) mental health (MH); and (8) role emotional (RE). Each of these eight health domains are divided into two summary components of physical (PCS) and mental summary scores (MCS), respectively. The score of each of the 8 domains of SF-8 HR-QOL were expressed as mean scores with standard deviation.[42]

Statistical methods

As a preliminary QOL clinical evaluation of the dietary supplement, a longitudinal design was used wherein, the differences between the SF-8 baseline scores at the time of entry and 6-months after CAM treatment in each test group of all patients, genders, ages, and different CAM treatment groups were evaluated using the 95% confidence intervals of all pre- and post-treatment groups. Statistical significance was implied a *P*-values <0.05 whenever the 95% confidence interval value that showed the exclusion of the value 0. All statistical analysis was carried out using the software package StatView 5.0 (Abacus Contents, Berkley, CA, USA).

Results

The total number of patients enrolled for HR-QOL assessment was 78. Subsequently, four patients were disqualified owing to invalid response to the questionnaire, and additionally, seven patients decided to discontinue the study for the reasons unknown. The remaining 67 patients have completed the study (compliance rate of 85.0%).

Demographic and clinical characteristics of patients show only the patients, who have complied satisfactorily and completed the HR-QOL study. The 67 patients had a mean age of 65.4 ± 10.8 with ages ranging between 29 and 79. The gender distribution of male and female was 38 and 29, respectively. Previous to the CAM treatment, the 67 cancer patients were diagnosed with the following cancers: prostate (31), endometrial (11), bladder (7), ovarian (5), cervical (5), gastric (2) and other cancers (6) that included endometrial stromal sarcoma (1), uterine sarcoma (1), vaginal cancer (1), oral cavity cancer (1), breast cancer (1) and renal cell carcinoma. All selected patients were previously treated with multiple combination of surgery, chemotherapy and radiation therapy (Table 2) and were clinically diagnosed as being in remission for 30 days prior to initiation of Sen-Sei-Ro treatment.

Table 2 Demographic and clinical characteristics of patients previously treated.

Number of patients	67
Age (year)	
Mean ± standard deviation	65.4 ± 10.8
Range	29–79
Gender (Male/female)	38/29

Diagnosis	Number of patients
Prostate cancer (early/advance)	31 (31/0)
Endometrial cancer (early/advance)	11 (8/3)
Bladder cancer (early/advance)	7 (6/1)
Ovarian cancer (early/advance)	5 (3/2)
Cervical cancer (early/advance)	5 (3/2)
Gastric cancer (early/advance)	2 (2/0)
Others (number of patients) (early/advance)	6 (2/4)
Endometrial stromal sarcoma (1), Uterine sarcoma (1), vaginal cancer (1), Oral cavity cancer (1), breast cancer (1), Renal cell carcinoma (1)	

Previous treatment	Number of patients
Operation	50
Chemotherapy	15
Radiotherapy	25

To evaluate HR-QOL effects of Sen-Sei-Ro, the 67 cancer patients were grouped as follows: (1) all patients group (67 patients); (2) gender difference (38 males and 29 females); (3) two-age groups (≤65 and ≥66), and (4) dose response groups. All of the descriptive statistical analysis from these studies for the PCS and MCS component summaries and the individual components are presented in Table 3. Two of the four of the physical component summaries, physical functioning and role functioning-physical before and 6-month after treatment were statistically significant ($P < 0.05$), while three of the four mental component summaries, social function, mental health, and emotional role before and 6-month after treatment were significantly improved ($P < 0.05$). Thus, HR-QOL among cancer patients in remission taking Sen-Sei-Ro significantly improved through 6 months following the last cancer treatment. Furthermore, PCS (physical component summary) showed statistically significant, while MCS (mental component summaries) showed no statistical significance before and 6-month after the treatment.

HR-QOL effects of the treatment in gender and age differences demonstrated that the male patients ($n = 38$) showed

Table 3 QOL assessed in cancer patients in remission before and after Sen-Sei-Ro, Powder treatment.

SF8-components	Variable	Before	After	Difference	95% confidence interval
Q1. General health (all patient: $N=67$)		51.1 ± 5.5	52.0 ± 6.5	0.913	−0.665 to 2.491
Gender	Male ($N=38$)	52.0 ± 5.3	53.0 ± 5.4	1.094	−0.565 to 2.752
	Female ($N=29$)	49.9 ± 5.7	50.6 ± 7.7	0.676	−2.389 to 3.741
Age	< 65 years ($N=26$)	49.5 ± 6.4	51.0 ± 7.3	1.483	−1.449 to 4.414
	> 66 years ($N=41$)	52.0 ± 4.7	52.6 ± 6.0	0.551	−1.337 to 2.440
Intake	1 pack/day ($N=23$)	53.4 ± 4.2	52.0 ± 7.3	1.434	−1.163 to 4.030
	2 pack/day ($N=22$)	49.5 ± 6.1	52.3 ± 5.9	2.762	0.916–4.608*
	3 pack/day ($N=22$)	50.1 ± 5.6	51.7 ± 6.6	1.517	−2.097 to 5.132
Q2. Physical function (all patient: $N=67$)		47.6 ± 7.3	50.1 ± 5.3	2.538	0.801–4.275*
Gender	Male ($N=38$)	48.9 ± 5.6	50.7 ± 4.9	1.874	0.543–3.206*
	Female ($N=29$)	45.9 ± 8.9	49.3 ± 5.9	3.408	−0.329 to 7.144
Age	< 65 years ($N=26$)	47.1 ± 8.9	50.6 ± 5.2	3.542	−0.107 to 7.191
	> 66 years ($N=41$)	47.9 ± 6.2	49.8 ± 5.5	1.901	0.126–3.676*
Intake	1 pack/day ($N=23$)	46.7 ± 6.5	49.7 ± 5.6	3.002	0.310–5.694*
	2 pack/day ($N=22$)	48.4 ± 5.4	51.2 ± 3.8	2.772	0.199–5.346*
	3 pack/day ($N=22$)	47.7 ± 9.6	49.6 ± 6.4	1.819	−2.252 to 5.889
Q3. Role physical (all patient: $N=67$)		47.9 ± 7.3	50.7 ± 5.5	2.818	1.084–4.552*
Gender	Male ($N=38$)	49.3 ± 6.0	51.6 ± 4.7	2.332	0.678–3.985*
	Female ($N=29$)	46.1 ± 8.5	49.6 ± 6.4	3.456	−0.050 to 6.962
Age	< 65 years ($N=26$)	46.9 ± 8.6	50.3 ± 6.4	3.460	−0.203 to 7.123
	> 66 years ($N=41$)	48.5 ± 6.5	50.9 ± 4.9	2.412	0.639–4.185*
Intake	1 pack/day ($N=23$)	48.2 ± 6.8	50.6 ± 5.6	2.396	−0.550 to 5.341
	2 pack/day ($N=22$)	48.1 ± 6.0	52.4 ± 3.1	4.295	1.783–6.807*
	3 pack/day ($N=22$)	47.4 ± 9.2	49.2 ± 6.9	1.784	−2.044 to 5.612
Q4. Bodily pain (all patient: $N=67$)		50.8 ± 10.4	53.5 ± 9.1	2.676	−0.016 to 5.368
Gender	Male ($N=38$)	54.7 ± 7.9	57.2 ± 5.6	2.520	0.044–4.996*
	Female ($N=29$)	45.8 ± 11.1	48.7 ± 10.4	2.881	−2.658 to 8.420
Age	< 65 years ($N=26$)	49.5 ± 11.9	51.4 ± 10.4	1.863	−3.341 to 7.066
	> 66 years ($N=41$)	51.7 ± 9.3	54.8 ± 8.0	3.192	0.091–6.293*
Intake	1 pack/day ($N=23$)	49.8 ± 11.8	52.4 ± 9.3	2.577	−2.677 to 7.832
	2 pack/day ($N=22$)	51.5 ± 9.1	53.4 ± 9.6	1.870	−3.290 to 7.029
	3 pack/day ($N=22$)	51.2 ± 10.3	54.8 ± 8.5	3.586	−0.647 to 7.820
Q5. Vitality (all patient: $N=67$)		51.8 ± 5.3	52.9 ± 5.4	1.085	−0.501 to 2.671
Gender	Male ($N=38$)	52.3 ± 5.1	53.8 ± 5.2	1.535	−0.567 to 3.636
	Female ($N=29$)	51.3 ± 5.6	51.8 ± 5.7	0.496	−2.056 to 3.047
Age	< 65 years ($N=26$)	50.6 ± 5.8	53.4 ± 4.6	2.889	0.440–5.338*
	> 66 years ($N=41$)	52.6 ± 4.8	52.6 ± 5.9	−0.059	−2.137 to 2.019
Intake	1 pack/day ($N=23$)	53.2 ± 4.6	52.7 ± 6.2	−0.429	−2.939 to 2.081
	2 pack/day ($N=22$)	50.7 ± 5.4	53.5 ± 4.4	2.812	0.445–5.178*
	3 pack/day ($N=22$)	51.6 ± 5.8	52.5 ± 5.8	0.941	−2.591 to 4.473

Table 3 (*Continued*)

SF8-components	Variable	Before	After	Difference	95% confidence interval
Q6. Social functioning (all patient: $N = 67$)		48.6 ± 7.5	50.9 ± 7.5	2.287	0.133—4.441*
Gender	Male ($N = 38$)	48.8 ± 7.3	51.7 ± 5.4	2.871	0.272—5.470*
	Female ($N = 29$)	48.3 ± 7.9	49.8 ± 9.6	1.521	−2.284 to 5.327
Age	< 65 years ($N = 26$)	47.6 ± 8.0	49.6 ± 10.1	2.063	−2.111 to 6.236
	> 66 years ($N = 41$)	49.3 ± 7.2	51.7 ± 5.3	2.429	−0.054 to 4.912
Intake	1 pack/day ($N = 23$)	49.2 ± 7.8	52.5 ± 6.3	3.367	−0.730 to 7.464
	2 pack/day ($N = 22$)	47.7 ± 7.9	50.8 ± 7.2	3.087	−0.856 to 7.031
	3 pack/day ($N = 22$)	48.9 ± 7.0	49.2 ± 8.9	0.358	−3.246 to 3.962
Q7. Mental health (all patient: $N = 67$)		49.8 ± 6.6	51.8 ± 5.7	2.021	0.228—3.814*
Gender	Male ($N = 38$)	51.5 ± 5.3	52.4 ± 5.6	0.943	−0.960 to 2.846
	Female ($N = 29$)	47.6 ± 7.5	51.0 ± 5.7	3.434	0.044—6.824*
Age	< 65 years ($N = 26$)	47.5 ± 7.8	51.9 ± 6.1	4.382	0.872—7.891*
	> 66 years ($N = 41$)	51.3 ± 5.2	51.8 ± 5.4	0.525	−1.370 to 2.419
Intake	1 pack/day ($N = 23$)	50.3 ± 8.0	52.3 ± 5.7	1.988	−1.603 to 5.580
	2 pack/day ($N = 22$)	48.6 ± 5.5	52.8 ± 4.7	4.232	1.439—7.026*
	3 pack/day ($N = 22$)	50.5 ± 6.0	50.4 ± 6.4	−0.155	−3.219 to 2.909
Q8. Role emotional (all patient: $N = 67$)		49.5 ± 6.6	51.6 ± 4.3	2.065	0.308—3.821*
Gender	Male ($N = 38$)	50.3 ± 5.1	51.5 ± 4.9	1.188	−0.941 to 3.317
	Female ($N = 29$)	48.4 ± 8.1	51.7 ± 3.5	3.213	0.161—6.266*
Age	< 65 years ($N = 26$)	48.2 ± 8.5	51.8 ± 3.5	3.584	0.293—6.874*
	> 66 years ($N = 41$)	50.3 ± 5.0	51.4 ± 4.8	1.101	−0.936 to 3.138
Intake	1 pack/day ($N = 23$)	49.7 ± 5.8	52.3 ± 3.3	2.641	−0.237 to 5.519
	2 pack/day ($N = 22$)	49.8 ± 4.5	51.2 ± 5.4	1.436	−1.332 to 4.204
	3 pack/day ($N = 22$)	49.0 ± 8.9	51.1 ± 4.2	2.091	−1.796 to 5.978
Summary score: PCS (all patient: $N = 67$)		47.8 ± 8.0	50.2 ± 7.9	2.345	0.331—4.358*
Gender	Male ($N = 38$)	49.8 ± 5.9	52.1 ± 4.3	2.362	0.871—3.853*
	Female ($N = 29$)	45.3 ± 9.7	47.7 ± 7.9	2.321	−2.073 to 6.716
Age	< 65 years ($N = 26$)	47.3 ± 9.6	49.3 ± 6.9	2.054	−2.161 to 6.269
	> 66 years ($N = 41$)	48.2 ± 6.9	50.7 ± 6.2	2.529	0.428—4.630*
Intake	1 pack/day ($N = 23$)	47.7 ± 8.1	49.3 ± 7.1	1.595	−1.835 to 5.025
	2 pack/day ($N = 22$)	48.4 ± 5.8	51.1 ± 5.7	2.702	−0.095 to 5.499
	3 pack/day ($N = 22$)	47.5 ± 9.9	50.2 ± 6.8	2.771	−1.828 to 7.369
Summary score: MCS (all patient: $N = 67$)		49.6 ± 5.7	51.0 ± 5.3	1.434	−0.277 to 3.146
Gender	Male ($N = 38$)	49.9 ± 5.0	50.8 ± 5.4	0.907	−1.358 to 3.171
	Female ($N = 29$)	49.2 ± 6.6	51.3 ± 5.3	2.126	−0.629 to 4.881
Age	< 65 years ($N = 26$)	47.7 ± 5.8	51.2 ± 5.1	3.498	0.797—6.200*
	> 66 years ($N = 41$)	50.8 ± 5.4	50.9 ± 5.5	0.126	−2.078 to 2.329
Intake	1 pack/day ($N = 23$)	50.6 ± 7.0	52.3 ± 4.8	1.744	−1.560 to 5.049
	2 pack/day ($N = 22$)	48.3 ± 5.1	51.1 ± 5.8	2.745	−0.458 to 5.948
	3 pack/day ($N = 22$)	49.9 ± 4.7	49.6 ± 5.3	−0.200	−2.884 to 2.484

* The exclusion of the value 'zero' in the 95% Confidence Interval implies a *P*-value less than 0.05.

statistical significance ($P < 0.05$) in 3 out of 4 physical components, physical function, physical role, and bodily pain, and only one mental component, social function. The physical component summary score was statistically significant ($P < 0.05$), while the mental component summary score was not. In contrast, the female patients ($n = 29$), statistical significance was seen with two mental components, mental health and the emotional role. However, the over-all mental component summary score was not statistically significant.

To evaluate whether or not age was a factor affecting the HR-QOL outcome the test material was arbitrarily divided into two age groups: ages less than 65 year old ($n = 26$) and ages greater 65 ($n = 41$). In the age group less than 65 ($n = 26$), statistical significance was seen in 3 out of the 4 mental components and MCS after 6-months of treatment ($P < 0.05$). In contrast, in the age group greater than 65 ($n = 41$), statistical significance was seen in 3 out of 4 physical components and PCS after 6-months of treatment ($P < 0.05$).

Furthermore, dose dependent HR-QOL effects were evaluated in 1 ($n = 23$), 2 ($n = 22$), and 3 pack per day ($n = 22$) for 6-month treatment, respectively. HR-QOL effects in all dose groups appeared to show improvement, however, statistical significance ($P < 0.05$) was observed only in the 2-pack per day group. Three out of 4 physical components, general health, physical function, physical role and 2 of the 4 mental components were statistically significant, respectively ($P < 0.05$).

Discussion

The objective of the current clinical study was to evaluate the quality of life of cancer patients in remission before and after 6-months of *A. blazei* Murill, Sen-Sei-Ro consumption.

Five of the 8 HRQOL components appeared to be significantly improved in all patients ($n = 67$). Males ($n = 38$) and ages over 65 (all genders, $n = 41$) demonstrated improvements mainly in physical components, while females ($n = 29$) and ages under 65 (all genders, $n = 26$) showed improvements mainly in mental components, respectively. Prior to this study, a double blind placebo HRQOL study with gynecological cancer patients undergoing a combination of chemotherapy and Sen-Sei-Ro agaricus mushroom treatment demonstrated a significant improvement in quality of life parameters as compared to the placebo control. These significant improvements in both physical well being and emotional stability were associated with the concomitant increase in natural-killer cell activity and significant resistance to immunosuppression (e.g. decrease in lymphocyte numbers) following a combination chemotherapy.[38] Furthermore, a retrospective HRQOL study with Sen-Sei-Ro demonstrated greater improvements in functional well being than just relief of symptoms among cancer patients.[40]

A crucial factor in chemotherapy is timing. Most anticancer drugs are highly toxic consequently limiting both the treatment doses as well as the treatment frequencies. Although the maximally tolerated dose (MTD) is used to minimize toxicities, it is not possible to completely avoid various side effects during and after cancer chemotherapy. Anticancer drug-induced side effects are attributed primarily to oxidative cellular damage, and severe immunosuppression.

Thus, the improved HRQOL results documented in cancer patients in remission following daily intake of Sen-Sei-Ro could be attributed to reduction of oxidative damage,[20,21] enhancement of immune function[35–37] and prevention of anticancer drug-induced mutagenesis,[22–24] and carcinogenesis.[30] Furthermore, low molecular weight fractions in Sen-Sei-Ro has been shown to inhibit activation of oncogenes by NNK, a potent cigarette carcinogen.[30]

The current preliminary HRQOL clinical study of cancer patients (67 subjects) in remission showed that daily intake of Sen-Sei-Ro appears to improve both physical and mental components based on SF-8 qualimetric analysis. However, this was a longitudinal clinical study lacking a placebo group. Therefore one cannot exclude the possibility that the improved HRQOL (at 6 months) results could be attributed partly to spontaneous recovery. Cancer patients in complete remission after successful treatment have been shown to be immunosuppressed long after chemotherapy (attributed most likely to either a single or combination chemotherapy). Furthermore, it is shown that more prior treatment results in a higher the degree of immunosuppression.[43,44] Higher incidence of relapse during the first 5-years of cancer remission could be attributed to a long term immunosuppression and/or immunologically compromised state. Daily use of Sen-Sei-Ro, may enhance immune function thus preventing or reducing incidence of cancer relapse.

Currently, there is no well-established HRQOL instrument to evaluate the magnitude of benefits from dietary supplements in cancer patients. The first goal is to create and validate an instrument targeted specifically to detect HRQOL benefits of Sen-Sei-Ro for cancer basing this on what current users perceive. The second goal is to get preliminary measurements of what benefits Sen-Sei-Ro has and to what extent. This would be ascertained using a well-established, validated quality of life instrument for cancer patients, the EORTC QLQ C30, and the new instrument that was developed. These results will allow us to accomplish the third goal, the final design of an efficient, adequately powered trial of Sen-Sei-Ro. Using the information from the initial group of 200 patients, 100 each in the Sen-Sei-Ro and placebo arms, we will be able to determine the ultimate size of the study needed to identify the effects of Sen-Sei-Ro.

In conclusion, the current findings are highly preliminary and need to be validated by a double blind placebo-controlled clinical study with a well-validated QOL instrument such as EORTC QLQ-C30 for various cancer categories. Our goal is to develop a quality of life instrument sensitive enough to measure HRQOL benefits of Sen-Sei-Ro, an immunomodulator in cancer patients undergoing chemotherapy.

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Conflict of interest statement

All authors have no financial relationships to disclose.

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