Bimonthly *CLINICAL PHARMACOLOGY AND THERAPY*
Yakuri to Rinsho®
• Vol. 14/No. 3/May 2004 Reprint

The Life Prolongation and QOL Improvement Effect of Rice Bran Arabinoxylan Derivative (MGN-3, BioBran) for Progressive Cancer

Kihachiro TAKAHARA and Kamataro SANO
Sano Surgery Clinic

©IYAKU SHUPPAN CO.

The Life Prolongation and QOL Improvement Effect of Rice Bran Arabinoxylan Derivative (MGN-3, BioBran) for Progressive Cancer

Kihachiro TAKAHARA and Kamataro SANO
Sano Surgery Clinic

Abstract

The present study was designed to determine whether or not the administration of MGN-3 could have its apothanasia effect and improve the QOL for 205 progressive and partially metastasized cancer patients in late III-IV stages after surgery. MGN-3 is a rice bran arabinoxylan derivative and known to have immunomodulation activity. The participants in this clinical study are hospitalized patients in our clinic treated with complementary alternative medicines (we call it "Non-Conventional Therapy") and anticancer medicines with lesser side effects. The 205 patients hospitalized for 6 months were grouped into two groups, viz, 109 patients (control group) treated with our standard complementary alternative medicines, and 96 patients who were further given MGN-3 (MGN-3 group) for one year and a half.

All the patients were measured for natural killer activity as an indication for the variation of immunoparameters. Simultaneously, the QOL of the patients was also checked. The NK cell activities of the patients after surgery were low on average; however, by the administration of MGN-3, NK activity was observed to increase and the apothanasia ratio also increased; the higher the patient NK activity is, the higher the apothanasia ratio was observed to rise. The above findings indicate that NK activity can be used as a pathological index of progressive cancers. QOL improvement was also observed with the administration of MGN-3.

Key words: complementary alternative medicines, rice bran arabinoxylan derivative, natural killer activity, apothanasia effect

Introduction

We perform a complementary alternative therapy developed in our clinic on progressive cancer patients who have a metastasis or unresectable lesion after surgery to maintain high QOL and prolong their survival time, and have obtained good results. This therapy consists of hospitalization and home treatment. The mean duration of hospitalization is 1 month, during which patients are treated and trained for treatment at home. After discharge, they are based on home care and periodically visit the clinic for examination and treatment. This therapy causes

no large damage to patients in principle. The main aim of the therapy is to put cancer cells into the dormant state. Normally, this therapy should be tried in postoperative patients without recurrence or metastasis. In the present study, however, the life prolongation effect of MGN-3 (BioBran) was confirmed in 205 cancer patients in late III-IV stages, including those who had a metastasis or unresectable lesion left after surgery. The purpose of this study was to determine whether the addition of MGN-3 to our complementary alternative therapy prolongs the survival time and improves QOL by enhancing the original effect of the therapy.

Methods

1. Patients

Subjects were patients hospitalized in our clinic who were treated with a complementary alternative therapy developed in this clinic (Table 1) and anticancer drugs that induce less adverse reactions. They were 205 progressive-cancer patients in late III-IV stages, who had recurrence, unresectable lesions, or metastasis after surgery. The primary lesion was in the lung (31 patients), liver (18), uterus (7), breast (33), prostate (4), rectum (28), stomach (34), lymph node (11), and others (29).

Table 1 Details of Complementary Alternative Therapy

immuno-enhancement:	CDA-II (enzyme in urine), germanium
	mushroom polysaccharides, specific substance Maruyama (SSM) oriental medicines, Lymphocytes
diet therapy:	Gerson's special diet therapy, kale vegetable juice, vitamins
intra-intestinal environmental improvement:	probiotics, prebiotics
thermotherapy:	far infrared ray, thermotherapy with loquest leaves
blood catharsis:	SOD, coffee enema
psycho-therapy:	thoroughgoing of positive way of thinking by seminars/lectures

Table2 Patients participated in the clinical study, MGN-3 Group and Control Group

Cancer site	MGN-3 Group	Control Group
Lung	14	17
Liver	10	8
Uterine	7	0
Breast	18	15
Prostate	3	1
Large intestine	9	19
Stomach	15	19
Lymph nod	7	4
Others	13	26
Total	96	109
Sex	Male 55, Female 41	Male 59, Female 50
Average age	56.0	53.5

Table 3 Scoring of QOL checkpoints and levels

pain, malaise and nausea		appetite	
none:	0	no appetite:	0
scarcely:	1	scarcely:	1
fairly strong:	2	fairly:	2
strong:	3	good appetite:	3
very strong:	4	-	

2. Investigational substance

MGN-3 is a rice bran arabinoxylan derivative obtained by hydrolyzing hemicellulose of rice bran with many carbohydrases, which have an immunomodulatory effect[2-3], active-oxygen scavenging effect[4], blood-sugar controlling effect[5], and effect of reducing adverse reactions to anticancer drugs[6]. The brand name of MGN-3 is Lentin Plus 1000, manufactured by Daiwa Pharmaceutical Co., Ltd. (Tokyo).

3. Methods

A total of 205 patients who visited our clinic within about 6 months were randomly divided into 2 groups (the control and MGN-3 groups). The control group was given a treatment prescribed in our clinic, and the MGN-3 group was given MGN-3 in addition to the same clinic-prescribed therapy. The breakdown of the patients is shown in Table 2. MGN-3 at 1 g was given orally 3 times a day after meals. The observation period was 18

months, and the patients visited once a month during the period to determine the activity of natural killer cells (NK activity) as an immune parameter. Patients who stopped visits without notice were excluded as dropouts from the study. Patients' QOL was checked by observation and inquiry during the study. Pain, malaise, and vomiting were evaluated using 4 grades, and appetite assessed using 3 grades to compare the scores before and after treatment. Table 3 shows the details.

Table 4 Relation among total survival rate, NK activity and survival rates in 2 groups

Group	MGN-3 Group	Control Group
Total survival rate	52/96 (54.2%)	19/56 (35.8%)
NK activity category		
Less than 19.9%	17/40 (42.5%)**	2/16 (12.5%)
20%-40%	18/35 (51.4%)*	7/25 (28.0%)
More than 40%	17/21 (81.0%)	10/15 (66.7%)

※ significant to the control group $^{**}p < 0.01$ $^{*}p < 0.05$

Table 5 QOL amelioration

QOL	Pain			Malaise			Nausea			Appetite		
	BT	AT	%	BT	AT	%	BT	AT	%	BT	AT	%
Control group	2.9	2.5	-14.0	3.5	2.9	-17.1	2.5	2.9	-14.6	1.6	1.9	+15.6
MGN-3 group	2.2	1.9	-15.9	2.9	2.4	-17.3	2.3	2.0	-13.3	1.7	2.1	+24.2

Note; BT: Before treatment AT: After treatment

%: Amelioration degree = (Scores at initiation less scores at termination) divide by scores at initiation

(-): indicates negative factors (decrease), (+): indicates positive factors (increase).

Results

1. Subjects included in analysis

A total of 152 of 205 patients were eligible for analysis, including 96 in the MGN-3 group and 56 in the control group. The main reasons for dropout were that the prescribed treatment became impossible because of increased pain, malaise, and vomiting, and decreased appetite due to cancer progression in some cases, and that other patients were pessimistic and gave up the prescribed treatment. There were no dropouts in the MGN-3 group, and all patients were included in the analysis. In the control group, 53 patients, accounting for 49%, dropped out.

2. The number of survival patients and the survival rates at 18 months

The survival rate at 18 months of treatment was 54.2% for the MGN-3 group (52 patients) and 35.8% for the control group (19). An investigation showed that no dropout survived. This means that the survival rate for the control group was 17.4% of 109 patients at the start of study.

3. Changes in NK activity

After starting the study, patients had decreased, unchanged, or increased NK activity. In the MGN-3 group, the NK activity decreased in 45.9% of patients, was unchanged in 21.9%, and increased in 32.3%. In the control group, the NK activity decreased in 51.8%, was unchanged in 9.0%, and increased in 39.3%. There was no difference in patients with increase or decrease in NK activity between both groups, but the rate of patients with unchanged NK activity was higher in the MGN-3 group.

4. Relation between NK activity and life prolongation

The NK activity before completion of the study was classified into categories of ≤20%, 20%-40%, and ≥40% to compare the survival rates. As a result, the survival rate was higher in patients with higher NK activity in both groups. The results are shown in Table 4.

5. QOL

Table 5 shows mean QOL scores and improvements (%) before and after treatment for 96 patients in the MGN-3 group and 56 in the control group.

Improvement of QOL was observed in both the control and MGN-groups, suggesting that our clinic's complementary alternative therapy is effective in improvement of QOL for patients with progressive cancer. Especially, the MGN-3 group had a marked increase in appetite.

Conclusion

The life prolonging and QOL improving effects of MGN-3 were studied in progressive cancer patients given a clinic-prescribed therapy and those given the same therapy plus MGN-3. As a result, clear life prolongation and QOL improvement were observed. The mean duration of hospitalization was 1 month. Although the maintenance of patients was not perfect during the study, a total of 205 patients participated in the study, and data were obtained from 152 of them. This number is sufficient for statistical analysis. The patients' NK activity had clearly decreased, and the survival rate tended to be low in patients with decreased NK activity. The rate of patients with unchanged or increased NK activity was higher in the MGN-3 group than in the control group, resulting in a 1.5 times higher survival rate obtained in the former group. There are many reports on the NK activity modulating

effect of MGN-3, and the results of the present study supported the effect. With respect to QOL improvement, appetite clearly increased in the MGN-3 group. While 49% dropped out in the control group, there was no dropout in the MGN-3 group. This was at least in part because of the improvement of the nutritional state due to increased appetite.

The relation between the NK activity and immunity against a tumor is controversial, and the role of NK cells is not completely clear. However, it is considered a good indicator for the nutritional state in progressive cancer patients, because patients with NK activity above a fixed level are likely to survive for a longer time. To prevent NK activity from the decline and maintain it at a high level may lead to life prolongation.

MGN-3, which helps the maintenance and enhancement of patient's self-curative ability, can be a useful tool for complementary alternative therapy.

Finally, we would like to thank Daiwa Pharmaceutical for supplying MGN-3 (BioBran) and Mitsubishi Chemical Laboratory (B.C.L.) for cooperation in blood tests.

Bibliography

1) Hashimoto, K.: Hospital to achieve miracles jointly by patients and doctors, Methamol Publication, Tokyo, 1999

2) Ghoneum, M.: Enhancement of Human Natural Killer Cell Activity by Modified Arabinoxylan from Rice Bran (MGN-3). *INT.IMMUNOTHERAPY,* **XIV** (2): 89-99, 1998

3) Ghoneum, M. and A. Jewett: Production of TNF-α and IFN-γ from Human Peripheral Blood Lymphocytes by MGN-3, a Modified Arabinoxylan from Rice Bran. *Cancer Detection and Prevention*, 2000

4) Tazawa, K., et al.: Scavenging Activity of MGN-3 (Arabinoxylan from Rice Bran) with natural Killer Cell Activity on Free Radicals. *Biotherapy* **14**: 493-485, 2000

5) Ohara, I., R. Tabuchi and K. Onai: Effects of Modified Rice Bran on Serum Lipids and Taste Preference in Streptozotocin-Induced Diabetic Rats. *Nutrition Research.* **20** (1): 59-68, 2000

6) Jacoby, H., G. Wnorowski, K. Sakata and H. Maeda: The Effect of MGN-3 on Cisplatin and Adriamycin Induced Toxicity in the Rat. *Journal of Nutraceuticals Medical Foods*, **3** (4): 3-11, 2001

This paper is a translation of an article in *Clinical Pharmacology and Therapy*, Vol. 14/No. 3/May 2004.

Bimonthly CLINICAL PHARMACOLOGY AND THERAPY

薬理と臨床®

● VOL.14/NO.3/May 2004 別 刷

進行癌に対する米ぬかアラビノキシラン誘導体（MGN-3, バイオブラン） の延命効果およびQOL改善効果

医療法人三矢会　佐野外科病院
高原　喜八郎　　佐野　鎌太郎

医 薬 出 版

進行癌に対する米ぬかアラビノキシラン誘導体（MGN-3，バイオブラン）の延命効果およびQOL改善効果

医療法人三矢会　佐野外科病院
高原　喜八郎　　佐野　鎌太郎

キーワード：代替・補完療法，米ぬかアラビノキシラン誘導体，ナチュラルキラー細胞活性，延命効果

はじめに

我々は，癌の手術後，転移が認められる進行癌および完除不能な進行癌の患者に対し，当院で開発した代替･補完療法を施すことにより，高いQOLを保ちつつ，生存期間の延長を図ることで，実績をあげている。平均的な入院期間は1カ月で，その間，治療を受けつつ治療の訓練を受け，退院後は在宅療養と定期的な通院による検査と治療を基本としている。基本的にはこのような療法は患者に大きなダメージを与えることがなく，癌を休眠させることに主眼をおいた治療である。本来このような治療は，術後，再燃，転移のない状態で試みられるべきであるが，今回は手術後に転移のみられる例，手術を行ったが完除できなかった患者を含むstage Ⅲ後半からⅣに分類される205名の患者を対象として，MGN-3（バイオブラン）の延命効果の確認を行った。当院で開発し，実施している代替・補完療法にMGN-3を加えることにより，更に「火消し効果」が高まり，延命期間の延長と，QOLの改善が得られるかどうかを検討した。

試験方法

1．患　　者

当院の入院患者で当院で開発・実施する代替医療（**Table 1**）と副作用の軽い抗癌剤治療を受療する患者を対象とした。患者は手術を行った後再発し，または完除が不可能で一部転移が認められる進行癌でⅢ期後半からⅣ期の205名とした。原発巣は肺癌31名，肝癌18名，子宮癌7名，乳癌33名，前立腺癌4名，直腸癌28名，胃

The Life Prolongation and QOL Improvement Effect of Rice Bran Arabinoxylan Derivative (MGN-3, Bio Bran) for Progressive Cancer
Kihachiro TAKAHARA (Sano Surgery Clinic) et al.

Table 1 Details of Complementary Alternative Therapy

immuno-enhancement:	CDA-II (enzyme in urine),germanium mushroom polysaccharides, specific substance Maruyama(SSM) oriental medicines, Lymphocytes
diet therapy:	Gerson's special diet therapy, kale vegetable juice, vitamins
intra-intestinal environmental improvement:	probiotics, prebiotics
thermotherapy:	far infrared ray, thermotherapy with loquest leaves
blood catharsis:	SOD, coffee enema
psycho-therapy:	thoroughgoing of positive way of thinking by seminars/lectures

Table 2 Patients participated in the clinical study, MGN-3 Group and Control Group

Cancer site	MGN-3 Group	Control Group
Lung	14	17
Liver	10	8
Uterine	7	0
Breast	18	15
Prostate	3	1
Large intestine	9	19
Stomach	15	19
Lymph nod	7	4
Others	13	26
Total	96	109
Sex	Male 55, Female 41	Male 59, Female 50
Average age	56.0	53.5

癌34名，リンパ腺癌11名，その他29名であった。

2. 被験物質

MGN-3は米ぬかのヘミセルロースを複数のカーボハイドラーゼで加水分解することによって得られた米ぬかアラビノキシラン誘導体で免疫調節作用[2-3]や活性酸素除去作用[1]，血糖値調節作用[5]，抗癌剤の副作用軽減作用[6]を有している。商品名はレンチンプラス1000で大和薬品株式会社（東京）が製造している。

3. 試験方法

約6カ月間に来院した患者205名をランダムに2群に分け，対照群は，当院のメニューに従った治療群，MGN-3群は，当院のメニューにMGN-3投与をする群とした。内訳を**Table 2**に示す。MGN-3は，1日3回毎食後，1回1gを経口投与した。観察期間を18カ月とし，観察期間中は，毎月来院し，免疫パラメータの検査として，ナチュラルキラー細胞活性（NK活性）の測定を行った。連絡もなく来院が途絶えた患者はdrop

Table 3 Scoring of QOL checkpoints and levels

pain, malaise and nausea		appetite	
none:	0	no appetite:	0
scarcely:	1	scarcely:	1
fairly strong:	2	fairly:	2
strong:	3	good appetite:	3
very strong	4	–	

Table 4　Relation among total survival rate, NK activity and survival rates in 2 groups

Group	MGN-3 Group	Control Group
Total survival rate	52/96(54.2%)	19/56(35.8%)
NK activity category		
Less than 19.9%	17/40(42.5%)**	2/16(12.5%)
20%-40%	18/35(51.4%)*	7/25(28.0%)
More than 40%	17/21(81.0%)	10/15(66.7%)

※ significant to the control group　**$p<0.01$　*$p<0.05$

Table 5　QOL amelioration

QOL	Pain			Malais			Nausea			Appetite		
	BT	AT	%	BT	AT	%	BT	AT	%	BT	AT	%
Control group	2.9	2.5	-14.0	3.5	2.9	-17.1	2.5	2.9	-14.6	1.6	1.9	+15.6
MGN-3 group	2.2	1.9	-15.9	2.9	2.4	-17.3	2.3	2.0	-13.3	1.7	2.1	+24.2

Note; BT: Before treatment　AT: After treatment
%:Amelioration degree = (Scores at initiation less scores at termination) divide by scores at initiation
(-):indicates negative factors (decrease), (+):indicates positive factors (increase).

outとして，試験の対象外とした。またQOLのチェックは試験期間中，患者の観察と問診を行い記録した。痛み，倦怠感，吐き気を4段階，食欲を3段階に分け，試験開始時と最終時を比較した。詳細を**Table 3**に示す。

結　　果

1．試験対象者数

参加者205名中152名が，解析の対象となった。内訳は，MGN-3群96名，対照群56名であった。脱落（試験対象外）の理由は，主として加療にも関わらず癌の進行に伴う痛み・倦怠感・吐き気等の症状が強くなり，食欲も低下し，メニュー通りの治療が行えなくなった場合と，患者自身の無気力から厭世感がつのり，治療に対して消極的になったことで，メニューに従った治療を断念した場合であった。MGN-3群には，脱落者は存在せず，全員が試験の対象となったが，対照群は，53名49%の患者が脱落した。

2．18カ月後の生存者数と生存率

加療18カ月後の生存率は，MGN-3群52名54.2%，対照群19名35.8%であった。調査の結果，脱落者に生存者が存在しなかったことから，対照群の生存率は，試験開始時の109名に対しては17.4%であった。

3．NK活性の変動傾向

試験開始後のNK活性の変動は，下降，不変，上昇の3つのタイプに分けられた。MGN-3群は，下降傾向45.9%，不変21.9%，上昇傾向32.3%，control群は，下降傾向51.8%，不変9.0%，上昇傾向39.3%であった。下降傾向，上昇傾向に群間差は認められなかったが，不変のケースが，MGN-3群に多い傾向が認められた。

4．NK活性と延命の関係

試験終了前のNK活性を，20%以下，20%～40%，40%以上に分類し，延命率を比較した結果，いずれの群もNK活性が高い患者程，延命率が高かった。結果を**Table 4**に示す。

5. QOL

MGN-3群96名と対照群56名の試験前と後のQOLスコアの平均値を**Table 5**に示す。試験後の試験前に対する改善度をパーセントで示した。

QOLの改善は対照群とMGN-3群いずれにも認められ，当院の代替・補完療法のメニューが進行癌の患者のQOLの改善に有効であることが示唆された。特にMGN-3群においては食欲の改善が顕著に認められた。

結　　論

MGN-3（バイオブラン）の進行癌患者に対する延命効果とQOLの改善を，当院の代替・補完療法のメニューに追加することにより検討した結果，明らかな延命効果，QOLの改善が認められた。当院における平均入院期間は1カ月であり，実験期間中の患者の管理は完璧ではなかったが，実験に参加した患者は205名であり，データの対象となった患者は152名であったことから，統計的な条件は十分に備えていると考える。患者のNK活性は明らかに低下しており，NK活性が低下傾向にある患者程，生存率は低い傾向にあった。MGN-3の投与により，NK活性が不変，上昇する患者が多かったことが，1.5倍の生存率の差につながったものと考える。MGN-3のNK活性調節作用については多くの報告があるが，今回の試験結果もその作用を裏付ける結果となった。またQOLの改善については，MGN-3群において食欲増進が顕著に認められた。対照群において49％の患者が脱落したのに対し，MGN-3群においては脱落者が0であったことと，食欲増進による栄養状態の改善は無関係ではないと考える。

またNK活性と腫瘍免疫については，多くの論議がなされており，NK細胞の役割については未だ不明な点が多いが，進行癌においてNK活性は患者の栄養状態を反映する良好な指標となるものと考える。すなわちNK活性がある一定のレベル以上に保たれている患者は延命に対する率が高い傾向にあることから，進行癌の患者においてNK活性の低下を防ぎ高レベルに維持することが延命につながるものと考える。

MGN-3は，癌治療における患者の自己治癒力の維持と増進に働くものであり，代替・補完療法の強力な武器になるものと考える。

最後に，MGN-3（バイオブラン）を提供して頂いた大和薬品株式会社と血液の検査に多大な協力を頂いたMitsubishi Chemical Laboratory (B.C.L) に対し，感謝の意を表する。

文　献

1) Hashimoto K.: Hospital to achieve miracles jointly by patients and doctors, Methamol Publication, Tokyo, 1999
2) Ghoneum M.: Enhancement of Human Natural Killer Cell Activity by Modified Arabinoxylan from Rice Bran (MGN-3). *INT.IMMUNOTHERAPY,* **XIV**(2): 89～99, 1998
3) Ghoneum M. and A. Jewett: Production of TNF-α and IFN-γ from Human Peripheral Blood Lymphocytes by MGN-3, a Modified Arabinoxylan from Rice Bran. *Cancer Detection and Prevention*, 2000
4) Tazawa K. et al.: Scavenging Activity of MGN-3 (Arabinoxylan from Rice Bran) with natural Killer Cell Activity on Free Radicals. *Biotherapy*, **14**: 493～485, 2000
5) Ohara I., Tabuchi R. and K. Onai: Effects of Modified Rice Bran on Serum Lipids and Taste Preference in Streptozotocin-Induced Diabetic Rats. *Nutrition Research*, **20**(1): 59～68, 2000
6) Jacoby H., Wnorowski G., Sakata K. and H. Maeda: The Effect of MGN-3 on Cisplatin and Adriamycin Induced Toxicity in the Rat. *Journal of Nutraceuticals Medical Foods*, **3**(4): 3～11, 2001

The Life Prolongation and QOL Improvement Effect of Rice Bran Arabinoxylan Derivative (MGN-3, Bio Bran) for Progressive Cancer

Kihachiro TAKAHARA and Kamataro SANO
Sano Surgery Clinic

Abstract

The present study was designed to determine whether or not the administration of MGN-3 could have its apothanasia effect and improve the QOL for 205 progressive and partially metastasized cancer patients in stages late III-IV, after surgery. MGN-3 is a rice bran arabinoxylan derivative and known to have the immunomodulation activity. Participants in this clinical study are the hospitalized patients in our clinic treated with complementary alternative medicines (we call it "Non-Conventional Therapy") and anticancer medicines of lesser side effects. The 205 patients hospitalized for 6 months were grouped into two groups, viz. 109 patients (control group) treated with our standard complementary alternative medicines, and 96 patients who were further given with MGN-3 (MGN-3 group) for one year and half.

All the patients were measured for natural killer activity as an indication for the variation of immunoparameter. Simultaneously, the QOL of the patients were also checked. The NK cell activities of the patients after surgery were low on average, however by the administration of MGN-3, NK activity was observed increased and the apothanasia ratio also increased; higher the NK activity of patient is, higher the apothanasia ratio was observed. From the above findings, it indicates that the NK activity can be used as a pathological index of progressive cancers. The QOL improvement was also observed by the administration of MGN-3.

Key words: complementary alternative medicines, rice bran arabinoxylan derivative, natural killer activity, apothanasia effect