Avemar Granulate as
Dietary Food / Special Purpose
Food for Cancer
DISCLAIMER
Technology review is a brief report, prepared on an urgent basis, which draws on restricted reviews from analysis of pertinent literature, on expert opinion and / or regulatory status where appropriate. It has not been subjected to an external review process. While effort has been made to do so, this document may not fully reflect all scientific research available. Additionally, other relevant scientific findings may have been reported since completion of this review.

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Ministry of Health Malaysia

DISCLOSURE

The author / authors of this report has / have no competing interest in this subject and the preparation of this report is totally funded by the Ministry of Health, Malaysia.
EXECUTIVE SUMMARY

Introduction
Separated wheat germ is traditionally included in healthy foods, consumed or served as raw material for extracts rich in vitamin E. During the 1990s, a new, fermented wheat germ extract for human consumption was invented by Professor Máté Hidvégi in Hungary. The standardized manufacturing technology included the extraction of wheat germ, the fermentation of the extract, followed by separation of the fermentation liquid, microencapsulation, drying, and granulation. The resulting powder was named Avemar pulvis (or simply Avemar), and the granulate is also known as Avemar. For a 70-kg weight adult, the single daily dosage of Avemar contains 8.5 g of Avemar pulvis plus flavoring ingredients, such as fructose and arome. After being dissolved in 150 ml of cold water, Avemar should be drunk preferably before a meal. The product has been approved as a dietary food for special medical purposes in cancer patients by the National Institute of Food Safety and Nutrition of Hungary.

This review was requested by the Senior Director of the Food Safety and Quality Division, Ministry of Health Malaysia following a request to import Avemar granulate as a special purpose food for cancer patients.

Objective/aim
To assess the effectiveness, safety and cost-effectiveness of Avemar granulate as a dietary food / special purpose food for cancer.

Results and conclusions
Benefits to patients with colorectal cancer, head and neck cancer as well as post surgical cancer patients cannot be determined as the evidence are limited and of poor quality of evidence. Hence, further research into the role of Avemar as a dietary food / special purpose food in these areas is warranted.

Methods
Five articles were included that consists of five non-randomised clinical trials and comparative studies.

Literatures were searched through electronic databases specifically PubMed/Medline, Cochrane, OVID, INAHTA and also in general databases. Google was used to search as additional web-based information. In addition websites for existing HTA agency, society websites and cross-referencing of the articles retrieved were also carried out accordingly to the topic.

A critical appraisal of the retrieved papers was performed and the evidence level was graded according to the US/Canadian Preventive Services Task Force.
Avemar Granulate as Dietary Food / Special Purpose Food for Cancer

1. INTRODUCTION

Wheat germ, if left in flour, has an adverse effect on the functional properties of dough and therefore on breadmaking quality. Therefore, most wheat germ is milled as part of mill feed, and a smaller portion is separated during the milling process. Separated wheat germ is traditionally included in healthy foods, consumed or served as raw material for extracts rich in vitamin E.\(^1\) During the 1990s, a new, fermented wheat germ extract for human consumption was invented by Professor Máté Hidvégi in Hungary.\(^2\) The standardized manufacturing technology included the extraction of wheat germ, the fermentation of the extract, followed by separation of the fermentation liquid, microencapsulation, drying, and granulation. The resulting powder was named Avemar pulvis (or simply Avemar), and the granulate is also known as Avemar.\(^{1-2}\) For a 70-kg weight adult, the single daily dosage of Avemar contains 8.5 g of Avemar pulvis plus flavoring ingredients, such as fructose and arôme. After being dissolved in 150 ml of cold water, Avemar should be drunk preferably before a meal. The product has been approved as a dietary food for special medical purposes in cancer patients by the National Institute of Food Safety and Nutrition of Hungary.

This review was requested by the Senior Director of the Food Safety and Quality Division, Ministry of Health Malaysia following a request to import Avemar granulate as a special purpose food for cancer patients.

2. OBJECTIVE/AIM

To assess the effectiveness, safety and cost-effectiveness of Avemar granulate as a dietary food / special purpose food for cancer.

3. TECHNICAL FEATURES

The original composition of wheat germ is substantially modified due to extraction followed by fermentation; therefore, Avemar cannot be replaced by wheat germ, germinated wheat, or any extract or derivative of these. Methoxy-substituted benzoquinones, present originally in the crude wheat germ as glycosides and liberated as aglycones by glycosidases during fermentation, are the indicator compounds for quantitative standardization.\(^{1-3}\) Remarkable non-nutrients of wheat germ include the methoxy-substituted benzoquinones (0.04%), which are present as glycosides of the corresponding methoxyhydroquinones.\(^{1-5}\) Avemar is also characterized by its specific high performance liquid chromatography fingerprint spectra. Avemar is currently manufactured by Biromedicina in Hungary in a Good Manufacturing Practice (GMP) - certified pharmaceutical plant in the Kunfeherto-Kiskunhalas region.

4. METHODS

4.1. Searching

Electronic databases searched through the Ovid interface (examples);
- MEDLINE(R) In-process and other Non-Indexed Citations and Ovid MEDLINE(R) 1948 to present
EBM Reviews - Cochrane Central Register of Controlled Trials until 3rd Quarter 2013
EBM Reviews – Database of Abstracts of Review of Effects until 3rd Quarter 2013
EBM Reviews - Cochrane database of systematic reviews - 2005 to 2013
EBM Reviews - Health Technology Assessment – until 3rd Quarter 2013
NHS economic evaluation database – until 3rd Quarter 2013

Other databases (example):
- PubMed
- Horizon Scanning database (National Horizon Scanning Centre, Australia and New Zealand Horizon Scanning Network, National Horizon Scanning Birmingham)
- FDA website
- INAHTA
- MHRA

Google scholar was used to search for additional web-based materials and information.

Appendix 1 showed the detailed search strategies. Last search was conducted on 19th August 2013.

4.2. Selection

A reviewer screened the titles and abstracts against the inclusion and exclusion criteria and then evaluated the selected full-text articles for final article selection.

The inclusion and exclusion criteria were:

Inclusion criteria

<table>
<thead>
<tr>
<th>Population</th>
<th>patients who had cancer</th>
</tr>
</thead>
<tbody>
<tr>
<td>Interventions</td>
<td>Avemar, Avemar with surgery, Avemar with chemotherapy, avemar with standard cancer treatment</td>
</tr>
<tr>
<td>Comparators</td>
<td>Chemotherapy, radiotherapy, surgery</td>
</tr>
</tbody>
</table>
| Outcomes                 | a) Protective effects against cancer.  
b) ability to kill cancer cells  
c) decrease risk of developing cancer  
d) improve immune system |
| Study design             | Clinical trials, interventional studies, comparative studies, systematic reviews for efficacy and effectiveness. Case series, case reports for adverse events |

Exclusion criteria

| Study design | surveys, anecdotal, animal studies |
Relevant articles were critically appraised using Critical Appraisal Skills Programme (CASP) and evidence graded according to the US / Canadian Preventive Services Task Force (Appendix 2). Data was extracted and summarised in evidence table (see Appendix 3).

5. RESULTS AND DISCUSSION

The search strategy yielded a total of 215 relevant titles and 111 abstracts were screened using the inclusion and exclusion criteria. After screening, 82 abstracts were found to be irrelevant. In total five full text articles which met the inclusion/exclusion criteria and quality of studies were included in this systematic review.

5.1. EFFICACY/ EFFECTIVENESS

Five articles were included that consists of five non-randomised clinical trials and comparative studies.

Jakab F and Mayer A et al in 2007 reported a Phase II clinical trial to see whether Avemar adds any therapeutic benefit to surgery or chemotherapy in colorectal cancer. From 1998 to 1999, eighteen control and twelve consecutive colorectal patients were enrolled at the Uzsoki Teaching Hospital, Budapest. All patients underwent curative surgery. The control patients received no other therapy or adjuvant chemotherapy alone. The other group was given either 9 gm Avemar alone or Avemar plus adjuvant chemotherapy. The median follow up was nine months. No new metastases developed in the avemar group while on the contrary several new metastases developed in the control group.

Jakab F and Shoenfeld Y et al in 2003 reported an open-label comparative study of colorectal cancer patients from three oncological institutions at Uzsoki Teaching Hospital of Budapest, University of Szeged and University of Debrecen, Hungary to estimate the expected difference between the progression-free survivals of colorectal cancer patients receiving anticancer treatments alone or anticancer treatments supplemented with Avemar. Sixty-six colorectal cancer patients received Avemar supplement for more than six months and 104 patients served as controls (anticancer therapies alone): no statistical difference was noted in the time from diagnosis to the last visit between the two groups. Time-related events were measured from the date of diagnosis.

- End-point analysis revealed that progression-related events were significantly less frequent in the Avemar group
  - (new recurrences: 3.0% in Avemar group versus 17.3% in control group, P<0.01; new metastases: 7.6% in Avemar group versus 23.1% in control group, P<0.01; Deaths: 12.1% in Avemar group versus 31.7% in control group, P<0.01).
- Survival analysis showed significant improvements in the Avemar group regarding progression-free (P=0.0184) and overall survivals (P=0.0278) probabilities.
- Strong predictors of survival in a Cox’s proportional hazards model (variable follow-up) were UICC stage (Union for International Cancer Control staging) and Avemar treatment only.

The study was short termed; however, the authors suggested that continuous supplementation of anticancer therapies with Avemar for more than 6 months may have
potential benefits to patients with colorectal cancer. Further clinical studies are needed to confirm this.

A group of sixty patients aged 18–65 years affected by head and neck tumours (stage IIIa, IIIb, IV) were enrolled in a study by Sukkar SG et al in Italy. Patients were divided into two subgroups: group A (control group) or group B. Group A received conventional oncological treatment alone, and group B (Avemar group) were treated with the combination of Avemar and standard antitumor therapy. All the patients were either able to spontaneously eat or receive enteral nutrition and had life expectancies of at least three months. The study was conducted following an open-label protocol and included a medical physical examination of the patient at baseline and after sixty days. At each study time point patients filled in the Spitzer’s questionnaire for the evaluation of their QOL. After two months only fifty-five patients survived and could be evaluated (twenty nine in the control group and twenty six in the Avemar group). Each patient was checked for circulating concentrations of hydroperoxides using the FRAS III test. The results showed that:

- The levels of oxidative stress (OS) significantly decreased after two months in the group receiving Avemar (group).
- The value of Spitzer’s index was significantly higher in group B, attesting to an improved quality of life.

The study was short termed, however, it was suggested by the authors that treatment with Avemar as an adjuvant to standard oncological therapy may result in a greater subjective improvement in well-being of the patients than conventional antitumor therapies alone. Further clinical studies are needed to confirm this.

An open-label, randomized, pilot, phase II clinical trial was conducted by Demidov LV et al to assess the supportive value of Avemar in the postsurgical adjuvant setting, at the N. N. Blokhin Cancer Research Center in Moscow between 2000 and 2001. Postoperative patients were randomized to either dacarbazine (DTIC) plus Avemar (twenty six patients) or to dacarbazine (DTIC) alone (control- twenty six patients). Although the administration of Avemar lasted for twelve months to test if this dietary food had any effect on progression free survival, post study patients were followed up for about an additional 7-year period. At the end of the 7-year-long follow-up period:

- Log-rank analyses (Kaplan-Meier estimates) showed significant differences in both progression-free (PFS) and overall survival (OS) in favor of the Avemar group. Mean PFS: 55.8 months (Avemar group) versus 29.9 months (control group), p=0.0137.
- Mean overall survival: 66.2 months (Avemar group) versus 44.7 months (control group), p = 0.0298.

An open-label, matched-pair (by diagnosis, stage of disease, age, and gender) pilot clinical trial was conducted by Garami M et al to compare the results between the combined administration of the medical nutriment Avemar with cytotoxic drugs (intervention group) and the continued administration of standard anticancer drug (control group) to reduce the incidence of treatment-related febrile neutropenia in children with solid cancers. Twenty-two randomly chosen patients (11 pairs) with histologically proven different pediatric malignant solid tumors were enrolled in this study between December 1998 and May 2002. All of them had been treated at the Oncology Unit of the Second Department of Pediatrics at the Semmelweis University in Budapest. The results were as follows:
During the treatment (follow-up) period, there was no recognizable progression of the malignant disease,

whereas at end-point (Dec. 31, 2003), the number and frequency of febrile neutropenic events (the latter expressed as percentages of the total number of chemotherapy cycles) significantly differed between the two groups: 30 febrile neutropenic episodes (24.8%) in the Avemar group versus 46 (43.4%) in the control group (Wilcoxon signed rank test: \( z = 2.090; P = 0.037 \))

The study was short termed; however, the authors suggested that the continuous supplementation of Avemar may help to reduce the incidence of treatment-related febrile neutropenia in children with solid cancers. Further clinical studies are needed to confirm this.

5.2  SAFETY

There was no retrievable scientific evidence on the adverse events of Avemar granulate.

5.3  COST/COST-EFFECTIVENESS

There was no retrievable scientific evidence on the cost-effectiveness of Avemar granulate.

5.4  LIMITATIONS

Our study has several limitations. The selection of the studies and appraisal was done by one reviewer. Although there was no restriction in language during the search, only English full text articles were included in the report.

6.  CONCLUSION

Benefits of Avemar granulate as dietary food / special purpose food for cancer to patients with colorectal cancer, head and neck cancer as well as post surgical cancer patients cannot be determined as the evidence are limited and of poor quality. Most of the studies have small numbers of patients, are short termed, not randomised (except for the study by Demidov LV et al), no blinding and outcomes measurements such as reduction in tumour size (not given in measuring units) cannot be determined. Therefore, further research with high quality evidence in these areas is warranted.
7. REFERENCES


8. APPENDIX

8.1. Appendix 1: LITERATURE SEARCH STRATEGY

<table>
<thead>
<tr>
<th>Ovid MEDLINE® In-process &amp; other Non-Indexed citations and OvidMEDLINE® 1948 to present</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Tumor$.tw.</td>
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<tr>
<td>2. Cancer$.tw.</td>
</tr>
<tr>
<td>3. neoplasm$.tw.</td>
</tr>
<tr>
<td>4. neoplasia.tw.</td>
</tr>
<tr>
<td>5. (neoplasm$ adj1 benign).tw.</td>
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<td>6. 1 or 2 or 3 or 4 or 5</td>
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<td>7. Head.mp. and neck.tw. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept, rare disease supplementary concept, unique identifier]</td>
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<tr>
<td>8. Mouth.tw.</td>
</tr>
<tr>
<td>10. Oral.mp. or mouth cavity proper.tw. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept, rare disease supplementary concept, unique identifier]</td>
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<tr>
<td>11. vestibule of the mouth.tw.</td>
</tr>
<tr>
<td>15. Melanoma.tw.</td>
</tr>
<tr>
<td>16. (Malignant adj1 melanoma$).tw.</td>
</tr>
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<td>17. 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16</td>
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<td>18. 6 and 17</td>
</tr>
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<td>20. Avemar.tw.</td>
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<td>21. FWGE.tw.</td>
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<td>22. Triticum vulgaris.tw.</td>
</tr>
<tr>
<td>24. wheat germ agglutinin isolectin 1.tw.</td>
</tr>
<tr>
<td>25. wheat germ agglutinin isolectin 2.tw.</td>
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<td>27. (agglutinins adj1 wheat germ).tw.</td>
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<td>28. triticum vulgare lectins.tw.</td>
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<td>30. triticum.tw.</td>
</tr>
<tr>
<td>31. (triticum aestivum or spelta or vulgare or turgidum).mp. or durum.tw. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept, rare disease supplementary concept, unique identifier]</td>
</tr>
<tr>
<td>32. (durum adj1 wheat$).tw.</td>
</tr>
<tr>
<td>33. 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31 or 32</td>
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34. Oncology.mp. or standard therapy.tw. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept, rare disease supplementary concept, unique identifier]
35. Radical surgery.tw.
36. Chemotherap$.tw.
37. (Drug adj1 therap$).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept, rare disease supplementary concept, unique identifier]
38. Pharmacotherapy.tw.
40. 34 or 35 or 36 or 37 or 38 or 39
41. 18 and 33
42. 17 and 40
43. 41 and 42

**OTHER DATABASES**

<table>
<thead>
<tr>
<th>Database</th>
<th>Notes</th>
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<tbody>
<tr>
<td>EBM Reviews - Cochrane Central Register of Controlled Trials</td>
<td>Same MeSH, keywords, limits used as per MEDLINE search</td>
</tr>
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<td></td>
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<td>EBM Reviews - Cochrane database of systematic reviews</td>
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<tr>
<td>EBM Reviews - Health Technology Assessment</td>
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<td>PubMed</td>
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<tr>
<td>NHS economic evaluation database</td>
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<td>INAHTA</td>
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<td>FDA</td>
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</table>
8.2 HIERARCHY OF EVIDENCE FOR EFFECTIVENESS STUDIES

DESIGNATION OF LEVELS OF EVIDENCE

I  Evidence obtained from at least one properly designed randomized controlled trial.

II-I Evidence obtained from well-designed controlled trials without randomization.

II-2 Evidence obtained from well-designed cohort or case-control analytic studies, preferably from more than one centre or research group.

II-3 Evidence obtained from multiple time series with or without the intervention. Dramatic results in uncontrolled experiments (such as the results of the introduction of penicillin treatment in the 1940s) could also be regarded as this type of evidence.

III Opinions or respected authorities, based on clinical experience; descriptive studies and case reports; or reports of expert committees.

SOURCE: US/CANADIAN PREVENTIVE SERVICES TASK FORCE (Harris 2001)
### Evidence Table: Efficacy / Effectiveness

**Question:** Is Avemar effective as a complementary therapy for management and treatment of cancer.

<table>
<thead>
<tr>
<th>Bibliographic citation</th>
<th>Study Type / Methodology</th>
<th>LE</th>
<th>Number of patients and patient characteristics</th>
<th>Intervention</th>
<th>Comparison</th>
<th>Length of follow up</th>
<th>Outcome measures/ Effect size</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Jakab F, Mayer A, Hoffmann A and Hidvegi M. First clinical data of a natural immunomodulator on colorectal cancer, Hepato-Gastroenterology 47 (2007):393-395.</td>
<td>Phase II clinical trial to see whether avemar adds any therapeutic benefit to surgery or chemotherapy in colorectal cancer</td>
<td>II-1</td>
<td>18 control and 12 consecutive colorectal patients</td>
<td>9 gm Avemar 1-2 times daily or avemar plus adjuvant chemotherapy.</td>
<td>No other therapy or adjuvant chemotherapy alone</td>
<td>2 years</td>
<td>The main outcome was to see whether avemar was able to delay the occurrence of new metastases in adjuvant relapsed setting in colorectal cancer patients. No new metastases developed in the avemar group after one to 2 years follow-up compared to controls.</td>
</tr>
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| 2. Jakab F, Shoenfeld Y, Balogh A, Nichelatti M, Hoffmann A et al. A medical nutriment has supportive value in the treatment of colorectal cancer. British Journal of Cancer (2003) 89, 465 – 469 | open-label comparative study to estimate the expected difference between the progression-free survivals of colorectal cancer patients receiving Anticancer treatments alone or anticancer treatments supplemented with avemar. | II-1 | Between November 1998 and March 2001, colorectal cancer patients from three oncosurgical institutions (at Uzsoki Teaching Hospital of Budapest, University of Szeged and University of Debrecen, Hungary) entered the study, all the patients had to undergo curative surgery at the time of diagnosis of their disease. The two cohorts of patients (Avemar and ‘control’) were formed according to the patients’ preference. | Anticancer treatment plus Avemar (9 g once daily) | Anticancer therapies alone | About six months | All patients were evaluated at baseline, at the end of the first month, and every 12 weeks afterwards. Evaluation Tumour progression was defined as an increase of at least 25% in the overall area of the tumour size or the appearance of any new lesions. Deaths were also reckoned in progression. Time-related events were measured from the date of diagnosis.  
- End-point analysis revealed that progression-related events were significantly less frequent in the Avemar group  
  - (new recurrences: 3.0 vs 17.3%, P<0.01;  
  - new metastases: 7.6 vs 23.1%, P<0.01;  
  - Deaths: 12.1 vs 31.7%, P<0.01).  
- Survival analysis showed significant improvements in the Avemar group regarding progression-free (P=0.0184) and overall survivals (P=0.0278) probabilities.  
- Strong predictors of survival in a Cox’s proportional hazards model (variable follow-up) were UICC stage and Avemar treatment only.  

The authors suggested that continuous supplementation of anticancer therapies with Avemar for more than 6 months may be beneficial to patients with colorectal cancer in terms of overall and progression-free survival.
**Evidence Table: Efficacy / Effectiveness**

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</tr>
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</table>
| 3. Sukkar SG, Cella G, Overa GM et al. | A multicentric prospective open trial on the quality of life and oxidative stress in patients affected by advanced head and neck cancer treated with a new benzoquinone-rich product derived from fermented wheat germ (Avemar). Mediterra J Nutr Metab (2008) 1:37–42. DOI 10.1007/s12349-008-0008-4 | II-1 | 60 patients affected by head and neck tumours (stage IIIa, IIIb, IV) were enrolled | group B was treated with Avemar in addition to standard therapy. | Group A was treated with conventional oncological therapy alone | About 2 months | After 2 months only 55 patients survived and could be evaluated (29 in the control group and 26 in the Avemar group). Each patient was checked for circulating concentrations of hydroperoxides using the FRAS III test. **Results**  
- The levels of oxidative stress (OS) significantly decreased after 2 months in the group receiving Avemar (group).  
- The value of Spitzer’S index was significantly higher in group B, attesting to an improved quality of life. |
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</tr>
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</table>
| 4. Demidov LV, Manziuk LV, Kharkevitch GY et al. Adjuvant Fermented Wheat Germ Extract (Avemar™) Nutraceutical Improves Survival of High-Risk Skin Melanoma Patients: A Randomized, Pilot, Phase II Clinical Study with a 7-Year Follow-Up. Cancer Biotherapy & Radiopharmaceutica Is, 2008; Volume 23, Number 4, 2008. DOI: 10.1089/cbr.2008.0486 | In a randomized, pilot, phase II clinical trial: To find out the efficacy of adjuvant use of avemar | II-1 To be eligible for this study, patients had to have malignant skin melanoma with lymphatic metastases (stage III disease) proven by histology; a World Health Organization (WHO) performance status of 0, 1, or 2; adequate organ functions; and life expectation of at least 12 months. All of the patients had to undergo radical surgery, including the complete removal of the primary tumor with a further complete resection of the involved regional nodes (lymphatic metastases), resulting in a macroscopically disease-free state. | Chemotherapy with dacarbazine supplemented with Avemar | Chemotherapy with dacarbazine | 7 years | At the end of the 7-year-long follow-up period: 
- Log-rank analyses (Kaplan-Meier estimates) showed significant differences in both progression-free (PFS) and overall survival (OS) in favor of the avemar group. Mean PFS: 55.8 months (avemar group) versus 29.9 months (control group), p = 0.0137. 
- Mean OS: 66.2 months (avemar group) versus 44.7 months (control group), p = 0.0298. |
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</table>
| 5.Garami M, Schuler D, Babosa M et al. Fermented Wheat Germ Extract Reduces Chemotherapy-Induced Febrile Neutropenia in Pediatric Cancer Patients. Pediatr Hematol Oncol, 2004; Volume 26, Number 10. | An open-label, matched-pair (by diagnosis, stage of disease, age, and gender) pilot clinical trial was conducted to compare the results between the combined administration of the medical nutriment Avemar with cytotoxic drugs (intervention group) and the continued administration of standard anticancer drug (control group) to reduce the incidence of treatment-related febrile neutropenia in children with solid cancers. | II-1 | Twenty-two randomly chosen patients (11 pairs) with histologically proven different pediatric malignant solid tumors were enrolled in this study between December 1998 and May 2002. All of them had been treated at the Oncology Unit of the Second Department of Pediatrics at the Semmelweis University in Budapest. | Standard anticancer drugs with avemar | Standard anticancer drugs | About two and half years | Results:  
- During the treatment (follow-up) period, there was no progression of the malignant disease,  
- Whereas at end-point the number and frequency of febrile neutropenic events significantly differed between the two groups: 30 febrile neutropenic episodes (24.8%) in the MSC group versus 46 (43.4%) in the control group (Wilcoxon signed rank test, \( P < 0.05 \)).  
The authors suggested that The continuous supplementation of anticancer therapies with the medical nutriment avemar helps to reduce the incidence of treatment-related febrile neutropenia in children with solid cancers. |

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