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Preclinical and clinical expert report for efficiency and safety of nutrient additive MAOLO on the hemopiesis in patients with oncological diseases, undergoing chemotherapy.

Seal [Medical University Sofia, Pharmaceutical Faculty]

Preclinical expert report for safety of the nutrient additive MAOLO

The preclinical safety data are based on an experimental study of nutrient additive MAOLO in Department "Pharmacology, pharmacotherapy and toxicology" of Pharmaceutical faculty of the Medical University – Sofia.
The nutrient additive has been studied for acute toxicity on laboratory animals – male and female mice and for cytotoxicity on human cellular line (HT-29). The studied product has been introduced once perorally in doses 5000 mg/kg and 10 000 mg/kg body mass (b.m.) of 36 male and female mice, line H. The introduction is peroral since this is the way of applying the nutrient additives in people. Every animal has been observed for 14 days for change in the general condition and lethal outcome. It has been found that the LD50 dose (the dose causing the death of 50% of the test animals) in MAOLO is more than 10 000 mg/kg b.m. As per the classification of Hodge and Sterner (Hodge H.C. & Sterner J.H., (1943). Determination of substance acute toxicity by LD50. Am. Ind. Hyg. Assoc. 10: 93-96) this value applies to class V, i.e. to the group of practically non-toxic substances. For cytotoxicity study, the nutrient additive MAOLO has been applied in in vitro model of human intestinal epithelium (cellular line HT-29). The results display that MAOLO is non-toxic in terms of this human cellular line, even when applying supraphysiological concentrations. A conclusion has been made that the product submitted –nutrient additive MAOLO is practically non-toxic in peroral application on male and female white mice and shows no toxicity in in vitro model of human intestinal epithelium (cellular line HT-29).

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Clinical expert report for efficiency and safety of the nutrient additive MAOLO

The efficiency of MAOLO in clinical conditions has been tested in total of 8 specialized oncological units in 7 cities in Bulgaria. The first observations of MAOLO capsules date back to August 2009 and the last ones have ended in January 2019. The nutrient additive MAOLO has been applied in total of 9 of the most frequent oncological diseases in Bulgaria. These are solid tumors, affecting the lungs, mammal gland, uterine cervix, colon and rectum, pancreas as well as malignant hematological diseases – non-Hodgkin lymphoma, Hodgkin disease, lymphoplasmocyte lymphoma. The nutrient additive has been applied in total of 559 hospitalized and ambulatory patients. The effect of MAOLO on the hematological indicators mainly affected by the chemotherapy has been clinically and laboratory established – leucocytes, thrombocytes, hemoglobin. The daily dose, applied in these investigations varies from 1 capsule to 6 capsule (maximal dose) depending on the hematological indicators. The capsules MAOLO have been taken during or after feeding. The effect of the nutrient additive has been traced for a period of 7-15 days to more than 1 year in the various clinical observations. The applied initial dose varies between the various centers – 1 capsule, 2x1, 3x1, 3x2 capsules a day. If needed, the dose has been increased with 1-2 capsules for 24 hours to the maximal dose of 6 capsules a day. The normalization of the leucocytes after the applying of dose 1 capsule a day is reported slowly – hardly after a 10 days treatment.

After the performing of the chemotherapy, a need was declared to apply the nutrient additive MAOLO in the maximal dose of 3x2 capsules wth duration of minimum 10-20 days for increase of the values of the thrombocytes, neutrophils and hemoglobin. As a prevention, during the whole time of the cytostatic treatment, 1-2 capsules a days were applied.

As an effect of the intake of the nutrient additive on the hemopoiesis, normalized hemo-indicators were found or values reached which do not require the applying of other measures for improvement of the hemo indicators. If the target values have not been reached with the lower doses of the nutrient additive MAOLO, a maximal dose of 3x2 capsules a day was applied.

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After correction of the dose, values of the hemo-indicators have been reached which allow the performing of chemotherapy with no delay. No delay of the chemotherapy was required due to fall below the limit of leucocytes, thrombocytes and hemoglobin. MAOLO has a good leucostimulating effect in light and moderately heavy leucopenia and stabilization with trend to increase of the thrombocytes and neutrophils. The observed patients of various centers have had original values of the leucocytes between 1,5 and 3,2.10^9/L. the level of leucocytes is traced in a controlled manner within intervals of 7-10 days, usually between two infusions of the cytostatics. The leucocytes have increased above the referent 3,5.10^9/L in 5-7 days, in individual cases up to 10 days. In the prophylactic intake of 1-2 capsules a day, throughout the cytostatic treatment, the values of the leucocytes have reached to5-6.10^9/L, in individual cases more but within the referent limits. In ambulatory patients, whereat the leucocytes have been traced once a week, the leucocytes have stabilized above 3,5 g/L, at original values 1,8-2,9.10^9/L. And in this group of patients, the leucocytes have normalized reaching 4-5.10^9/L.

The last clinical observation of nutrient additive MAOLO has been performed in Complex Oncological Center – Ruse for a period of 4 months – from October 2018 to January 2019 of total of 39 patients. In this treatment, the effects of MAOLO have been compared to a control product with random signature SGN which has a composition and form enabling a comparative study with MAOLO. This enables the comparison to a similar product which has also been used in the same dose as MAOLO – 3x 2 capsules a day. This comparison is important since it enables to make a comparative conclusion regarding the effect of the two products on the hematological indicators and the need to use further measures for their stimulation. It also makes impression that in some of the patients taking SGN, the intake of MAOLO was necessitated. For patients who continued with the intake of SGN, no positive impact was reported of the hematological indicators. Besides, it has been evaluated that for these patients, the risk for complications as a result of induced bone marrow toxicity remained increased which may necessitate interruption of the chemotherapeutic treatment. In table 1, a comparison has been presented between MAOLO and SGN based on the observations.

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Table 1. Comparison between nutrient additive MAOLO and the product SGN.

Summary of the results for nutrient additive MAOLO

Place of performing the observation	Total number of patients and period of observation	Oncological disease	Number of patients	Daily dose and duration of the intake	Laboratory indicators	Effect of NA on the laboratory tests	Result on the chemotherapy
Complex oncological center (COC)-Ruse-EOOD Dr. Ivan Ivanov Dr. Valerii Yordanov	39 patients for 4 months – 10,11,12 2018 and 01.2019	Colorectal carcinoma	11	For 7 patients – 3x2 capsules (maximal dose) MAOLO during feeding	Hemo-indicators – leucocytes, thrombocytes, hemoglobin	Normalized hemo-indicators or values reached which do not require the application of other measures for improvement of the hemo-indicators	Not delayed and continued within schedule
		Lung carcinoma	7	Initially 3x1 capsule during feeding, in 5 of the patients after chemotherapy, the dose has been increased to 3x2		After dose correction, values of the hemo-indicators were reached which do not require the application of other measures for improvement of the hemo-indicators	Not delayed and continued within schedule
		Mammal gland carcinoma	4	Initial dose – 3x1 capsule during feeding; after performed chemotherapy, maximal dose 3x2 c was necessitated		After dose correction, values of the hemo-indicators were reached which allowed the performing of chemotherapy with no delay	Not delayed

Summary of the results for the product SGN

Complex oncological center (COC)-Ruse-EOOD Dr. Ivan Ivanov Dr. Valerii Yordanov	17 patients for 4 months – 10,11,12 2018 and 01.2019	Colorectal carcinoma	8 of SGN In 1 patient, replacement was needed of SGN with MAOLO (3x2c) due to bone marrow toxicity registered after the chemotherapy	3x2 capsules during feeding	Hemo-indicators – leucocytes, thrombocytes, hemoglobin	In 7 of the patients SGN did not essentially affect the hemopoiesis After replacement of SGN with MAOLO in 1 patient, the tested hemo-indicators have been normalized	The chemotherapy after replacement with MAOLO was not delayed and proceeded within schedule. After intake of SGN he chemotherapy was not delayed but the risk for complications remained high as a result of bone marrow toxicity induced by the chemotherapy
		Mammal gland carcinoma	9 patients In 5 patients replacement was needed of SGN with MAOLO 3x2c due to bone marrow toxicity after chemotherapy	3x2 capsules during feeding		For the patients with SGN, the hemopoiesis is not essentially affected For 3 patients the hemoglobin fell below the lower limit In 1 patient, except for the hemoglobin, the leucocytes are also below the lower limit. After replacement of SGN with MAOLO, the hemo-indicators were normalized.	The chemotherapy after replacement with MAOLO continued within schedule. After the intake of SGN, the chemotherapy even not delayed, increased the risk for complications due to bone marrow toxicity prevented by SGN at very low intensity.

The comparative study demonstrated that the product SGN does not possess the preventative, stimulating and normalizing effect on the hemopoiesis, as the original MAOLO. A conclusion can be drawn that the nutrient additive with the original name of MAOLO is efficient in the prevention of the bone marrow toxicity as a result of chemotherapy with hematoxic cytostatics by normalizing simultaneously and separately the observed hemo-indicators – leucocytes, thrombocytes and hemoglobin. In the statements of the clinical observations it has been noted that no unwanted drug reactions were found (even in treatment that lasted for 4-6 months) which are a result of the product application. The results display that the nutrient additive MAOLO prevents the use of expensive therapy with colon stimulating factors, transfusion of whole blood or thrombocyte mass aiming treatment of the cytotoxic complications and does not allow the interruption of te scheduled chemotherapy. Since MAOLO is a nutrient additive, the pre-clinical and clinical observations give better confidence to the doctors and patients that the product is with practically proven safety and efficacy as opposed to many other nutrient additives whereat such data is not known.

Sofia
20.11.2019

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