Evaluation of the thesis of Ludmila Lipska, MD "Colorectal carcinoma and markers of biological activity".

One of the most important qualifications of similarity of the title and the content of the thesis is fully achieved. The thesis is written in a concise way which is sometimes causing tables and figures would need explanation which is not available. For instance, it would have been more acceptable if some explanation was given about the results represented in graphs 1-9. Why is there an increase in the Age-Standardised Rate in Hungary (graph 3 exceeding Czech Republic), a decrease in the United States of America (graph 4) and a strong increase in Japan (graph 9)?

The introductory chapters about "Cancerogenesis" and "Genetics" are written extremely well leading to the description of the impact of "markers of biological activity". It is a pity that mostly the American spelling of "tumor" is used in stead of the British "tumour" (see chapters on page 23,24 and 26 with "tumor" but chapter on page 26 with "tumour".

On page 26 and 27 motives are given for the use of tumour markers (especially CEA) as prognostic markers in colorectal cancer. These motives are clearly described and fully acceptable in Dukes' C colorectal cancer patients. It would be interesting to know if the aggressive disease described in 40-50% of Dukes' B patients (which is a high percentage) is dealing with colonic and/or rectal carcinoma patients. It is not clear if adjuvant chemotherapy (as stated) has a modest but detectable beneficial effect. The American Society of Clinical Oncology published in 2004 the following recommendations: "The routine use of adjuvant chemotherapy for medical fit patients with stage II colon cancer is not recommended. However, there are populations of patients with stage II disease that could be considered for adjuvant therapy, including patients with inadequately samples nodes, T4 lesions, perforation, or poorly differentiated histology (Al B Benson III et.al. J Clin Oncology 2004; 22: 3408-3419).

The characteristics of the different types of biological markers are adequately described and could be very helpful chapters for students and physicians interested to apply tumour markers in clinical practice.

The decision to split the patient results in 2 groups makes these results and the contribution of the tumour markers very clear. The data handling is adequate and the statistical methods are applied correctly. The statement: "values equal to or less than 0.05 were considered as significant" is fully correct. However, the p-value in group 2 versus 3 in Table 19 for CA 19-9 is 0.052 and indicated as significant; the p-value in Table 21 for TPA 0.0522 is also indicated as significant. This would have been correct if the p-value would have been given as 0.05, because the round up downwards of 0.052(and of 0.0522) is 0.05. In itself 0.0522 is above 0.05 .In the discussion about the contribution of CA 242 (ref. 71 on page 76) p=0.053 is taken as borderline significant. This should not be promoted, but p-values slightly above 0.05 could be indicated as a trend for difference. Nevertheless, these small comments do not interfere with the principal results of the study.

The number of patients in some tables deserves further attention and some explanation. In Table 17 CEA is determined in 91 patients and Leptin in only 58 patients. Also in Table 27 there are 25 CEA determinations and only 12 ICAM determinations. What is the reason for these differences? Could these different numbers influence statistics?

It is of great interest that it is confirmed in this thesis that CEA, mucin markers (like CA 19-9 and CA 242) and cytokeratins (like TPA and TPS) behave differently and independently during follow up. The Chapter Results together with the Discussion and the Conclusions clearly indicate that the goal of this thesis was accomplished.
This thesis –written by an oncological surgeon- about the application of tumour markers and other markers of biological activity in colorectal cancer could have a very high impact on the acceptance of these markers in daily oncological practice.
This thesis should be successful and could obtain the qualification "***cum laude***".

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