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Tumor Type M2 Pyruvate Kinase in Colorectal Cancer: A Predictive Activity Marker versus Classical Mass Tumor Markers

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Recently, studies on pancreatic and renal carcinoma demonstrated a high clinical validity of the tumor M2 isoenzyme of pyruvate kinase (TuM2-PK) as marker of *tumor activity*. In a preliminary analysis, we investigated this new marker in 11 patients (pts) under adjuvant chemotherapy (Chx) and 29 pts with advanced colorectal cancer under different types of Chx. The clinical course of the disease was correlated to plasma TuM2-PK levels (normal <15 U/ml) and to serum CA19-9 (normal <37 U/ml) - and CEA (normal <2.5 ng/ml) levels as markers of *tumor mass*. Plasma and serum samples were taken at baseline before adjuvant or palliative Chx with the measurements being repeated at each Chx cycle. Response was assessed by clinical examination and standard imaging methods like ultrasound and CT scan. TuM2-PK was measured using a monoclonal antibody-based immuno-enzymetric assay (ScheBo®• Biotech AG, Giessen, Germany), while CA19-9 and CEA were determined on a chemilumine-scence basis (Bayer® Diagnostics, Tarrytown, USA). All pts under adjuvant Chx started with a slightly elevated baseline level with a maximum of 27 U/ml. Interestingly, all plasma levels normalized by the end of adjuvant Chx. In patients with stage IV disease, the median baseline (range) levels before Chx were at 183 U/ml (14–629) for TuM2-PK, at 1268 U/ml (5.7-8392) for CA19-9 and at 1397 U/ml (0.9-10006) for CEA. The correlation between TuM2-PK and the mass tumor markers CA19-9 and CEA was calculated at baseline with r= 0.3 and 0.7, respectively. CA19-9 and CEA correlated with an r=0.9. The comparison of TuM2PK and CA19-9 or CEA resulted in r-coefficients of (-)0.1 each for pts with stable disease and even in r= (-)0.4 each for remitting pts. The subgroup of pts with progressive disease kept positive r-coefficients between 0.3 and 0.6 for the comparison of all markers to each other. These results show an inverse behavior of the two mass markers as compared to TuM2-PK which generally had decreased by 58% at week 4 after Chx initiation for pts with benefit from Chx while the mass tumor markers showed a postponed decrease with a median change of just 20% after 4 weeks. The biochemical courses remained concordant in patients with progressive disease as tumor activity and tumor mass remain elevated simultaneously. These results fit with data from advanced breast cancer where TuM2PK was shown to be a predictive marker for benefit from systemic therapy as long as an increased baseline level normalized within 4 weeks after start of palliative Chx. The biochemical background for the prompt decrease of TuM2-PK in responding patients is probably based on a regulatory switch from the dimeric form to the tetrameric isoenzyme of pyruvate kinase.

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