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Intracellular signalling via the AKT axis and downstream effectors is active and prognostically significant in cancer of unknown primary (CUP): a study of 100 CUP cases.

Golfinopoulos V, Pentheroudakis G, Goussia A, Siozopoulou V, Bobos M, Krikelis D, Cervantes A, Ciuleanu T, Marselos M, Fountzilas G, Malamou-Mitsi V, Pavlidis N.

Source

Department of Medical Oncology, Ioannina University Hospital, Ioannina, Greece.

Abstract

BACKGROUND:

Hypothesising that cancer of unknown primary (CUP) may harbour unique characteristics, we present a translational study of the immunohistochemical expression and clinical correlation of key PTEN/AKT pathway molecules.

PATIENTS AND METHODS:

We collected 100 paraffin-embedded CUP tissue blocks. We studied using tissue microarrays the expression of PTEN, phospho-AKT, Cyclin D1, p21, phospho-RPS6. From the percentage of staining tumour cells and the literature, we selected cut-offs to classify the expression of each biomolecule. We correlated IHC expression with clinical data.

RESULTS:

PTEN, pAKT, and pRPS6 showed frequent expression. At univariate analysis, high IHC expression of pAKT and pRPS6 displayed statistically significant association with worse survival. Prognosis was worse upon concurrent high IHC expression of pMAPK and pAKT {median overall survival = 8 months [95% confidence interval (CI) 5.3-10.7] versus 17 months [95% CI 13.1-20.9]}. In multivariate analysis, high p21 was associated with better survival (risk ratio [RR] = 0.34 [95% CI 0.16-0.73], P = 0.005). High expression of pAKT (RR = 2.39 [95% CI 1.23-4.66], P = 0.01) or pRPS6 (RR = 2.76 [95% CI 1.31-5.84], P = 0.008) was associated with worse survival.

CONCLUSIONS:

p21 expression conferred favourable prognosis, while high pAKT or pRPS6 expression predicted worse prognosis. Concurrent MAPK and pAKT expression had a marked adverse impact on survival.