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Cancer Science & Pediatrics 2019: Negative prognostic significance of primary cilia, CD8+ tumor infiltrating lymphocytes and PD1+ cells expression in clear cell renal cancer - Josef Dvorak - Charles University and Thomayer Hospital, Czech Republi0063

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Statement of the Problem: Primary cilia are specialized sensory microtubulebased organelles that project from the surface of almost all human cells except hematopoietic cells. Primary cilia are considered to represent a functional homologue of the immune synapse due to morphological and functional similarities in architecture. The aim of this study was to investigate the potential association and combined prognostic significance of the frequency of primary cilia (PC), programmed cell death protein-1 receptor (PD1) and CD8+ tumor infiltrating lymphocytes (TIL) in patients with clear cell renal cancer (ccRCC). Methods: The frequency of PC, PD1 expression and the frequency of intratumoral CD8+TIL were evaluated in 104 ccRCC patients. Results: The expression of PD1+ cells was <5% in 52 patients, 5-25% in 34 patients and 26-50% in 13 patients and >50% in 5 patients. Intratumoral CD8+ TIL were evaluable in all patients: negative in 1 patient, <25% in 63, 26-50% in 29 and >50% in 11 patients, respectively. Overall survival (OS)

according to frequency of PC was significantly shorter in patients with higher frequency (≥0.002) than in patients with lower frequency (<0.002) (p<0.001). Median OS according to intratumoral CD8+ TIL expression was significantly shorter in patients with higher expression >25% median OS 4.6 years than Primary cilia (PC) are specialized sensory microtubule-based organelles that project from the surface of almost all human cells except hematopoietic cells [1,2]. PC are considered to represent a functional homologue of the immune synapse due to morphological and functional similarities in architecture. The immune synapse is a temporary interface between an antigen-presenting or cancer cell and the effector lymphocyte.

One mechanism by which cancer cells limit the formation of immune synapse is via upregulation of programmed death-1 ligand (PD-L1) and subsequent ligation to programmed death protein-1 receptor (PD1) on CD8+ tumor infiltrating lymphocytes (TIL). Both microtubule structures, i.e. primary cilia and immune synapses between cytotoxic CD8+ TIL and antigen-presenting or cancer cells, are regularly found in varying amounts in the microenvironment of solid tumors. Recently we reported the positive prognostic significance of primary cilia in tumor microenvironment in intestinal cancer. Favorable prognostic and predictive significance of high density of CD8+ TIL has been repeatedly demonstrated across a spectrum of different primary tumors with the exception of renal

in patients with lower expression <25% median OS 9.7 years (p=0.006). Median OS according to PD1+ expression was significantly shorter in patients with higher expression >25% median OS 2.9 years than in patients with lower expression <25% median OS 8.9 years (p=0.006). as in our previous studies, we have also been interested in the relationship between PC and immune synapses in tumor microenvironment. Simultaneous immunohistochemical demonstration of CD8+ TIL and PD-1 expression in tumor is a close approximation of the imaging of immune synapse. Clear cell RCC (ccRCC) is the most common. type of kidney cancer. Immunotherapy and targeted therapy have improved the outcome for metastatic ccRCC patients [14,15].
The aim of the present pilot study was to examine the association and correlate the prognostic significance of the frequency of PC, PD1+ cells expression and CD8+ TIL expression in the same. group of patients with ccRCC.

Conclusion & Significance: The present study provides the first data on the potential association and combined prognostic significance of frequency of PC, PD1+ cells and CD8+ TIL in patients with clear cell renal cancer. These findings are of importance considering the recent advances that introduced immunotherapy as a major approach in metastatic RCC.
celcarcinoma (RCC), where the high density of CD8+ TIL is a contrastingly negative prognostic factor.

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