PLASMA YKL-40 IS ASSOCIATED WITH PROGNOSIS IN PATIENTS WITH METASTATIC PANCREATIC CANCER RECEIVING IMMUNE CHECKPOINT INHIBITORS IN COMBINATION WITH RADIOThERAPY

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Background YKL-40, also known as chitinase-3 like-1 protein (CHI3L1), is a secreted glycoprotein produced by various cell types including stromal, immune, and cancer cells. It contributes to cancer progression through tumor-promoting inflammation. YKL-40 has been shown to inhibit the cytotoxic function of T and NK lymphocytes, and in vivo studies have demonstrated synergistic anti-cancer effects of blocking YKL-40 in combination with immune checkpoint inhibitors (ICIs). Biomarkers for the prediction of the response to ICIs are highly needed. We investigated the association between plasma YKL-40 levels and clinical benefit and survival in patients with metastatic pancreatic cancer (mPC) receiving ICIs combined with stereotactic body radiotherapy (SBRT).

Methods Blood samples were collected from 84 patients with mPC who participated in the randomized phase II CheckPAC study, in which patients received nivolumab with or without ipilimumab combined with a single fraction of SBRT (15 Gy). Blood samples were collected at baseline, after 2 weeks, and then every 8 weeks until disease progression. Plasma YKL-40 was measured using a commercial ELISA kit.

Results Median plasma YKL-40 was higher after 8 weeks of treatment in patients with progressive disease than in patients with clinical benefit, defined as stable disease, partial or complete response ($p < 0.05$). Elevated baseline plasma YKL-40 was an independent predictor of shorter overall survival (OS) (HR 2.06, 95% confidence interval 1.15–3.7). A ≥40% decrease in plasma YKL-40 was associated with longer OS ($p = 0.0025$) compared to stable (<40% decrease to ≤40% increase) and >40% increasing plasma YKL-40. There was no correlation between plasma YKL-40 and the tumor burden marker CA19–9 at baseline or during treatment.

Conclusions This study contributes new knowledge regarding plasma YKL-40 as a predictor of clinical benefit from ICIs combined with radiotherapy. These exploratory results warrant further investigation of YKL-40 as a biomarker for patients treated with immunotherapies.

Ethics Approval The CheckPAC study was approved by the Danish Ethics Committee (VEK, j.nr. H-16031247) and the Danish Data Protection Agency (j.nr. 2012–58–0004; HGH-2016–112; I-Suite j.nr. 05088).

Consent Signed informed consent was obtained from each participant.