Non-invasive biomarkers of ECM turnover are prognostic for combinations of checkpoint inhibition immunotherapy in solid tumors

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BACKGROUND

- Immune checkpoint inhibitors (ICIs) are being investigated in many different combinations (Table 1) but only a fraction of patients respond.
- Prognostic biomarkers are needed to assess the likelihood of benefit.
- Tumor fibrosis and the high collagen/ECM turnover in the tumor microenvironment – processes are closely related to response to ICIs and survival outcomes.
- Clinical utility of non-invasive biomarkers of collagen-1 (reC1M), collagen-III (PRO-C3), collagen-4 (C4M), collagen-19 (PRO-C19), collagen-20 (PRO-C20) and TGF-β activity in metastatic cancer patients treated with ICIs was investigated.

METHODS

- PRO-C3, PRO-C19, PRO-C20, TGF-β, reC1M and C4M were measured with ELISAs in pre-treatment serum from 33 patients with metastatic disease in a basket trial comprising 14 tumor types and 8 different checkpoint inhibition regimens (Table 1).
- The association between biomarker levels and overall survival (OS) outcome was evaluated by Kaplan-Meier analysis and Cox regression analysis after dichotomizing patients at the 75th percentile (Q4).

PATIENT / TREATMENT OVERVIEW

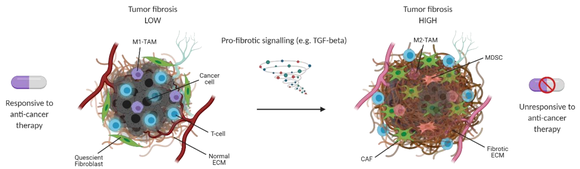
Cancer type	Number of patients	Treatment
Esophageal cancer	1	Nivolumab+Anti-LAG3
Breast cancer	2	Carboplatine+Gemcitabine+Pembrolizumab
Ovarian cancer	4	Atezolizumab+BET inhibitor
Parotid cancer	1	Nivolumab
Gastric cancer	2	Nivolumab+Anti-LAG3 or Atezolizumab+CD40-agonist
Bladder cancer	3	Pembrolizumab
Colorectal cancer	5	Nivolumab, Pembrolizumab, Atezolizumab++bispecific antibody targeting CEA and CD3 or Atezolizumab+CD40-agonist
HCC	3	Nivolumab+Anti-LAG3
Colorectal cancer	1	Atezolizumab+bispecific antibody targeting CEA and CD3
Mesothelioma	2	Pembrolizumab or Atezolizumab+CD40-agonist
Neuroendocrine tumor	1	Pembrolizumab
NSCLC	5	Nivolumab, Pembrolizumab or ipilumumab+Nivolumab
Pancreas adenocarcinoma	1	Atezolizumab+CD40-agonist
UPT	2	Atezolizumab+bispecific antibody targeting CEA and CD3 or Pembrolizumab

CONCLUSION

Across a diverse cohort of patients with metastatic cancer treated with different checkpoint inhibition regimens, non-invasive biomarkers associated with tumor fibrosis and collagen/ECM turnover (PRO-C3, PRO-C19, PRO-C20, TGF-β, reC1M and C4M) could identify cancer patients with poor prognosis

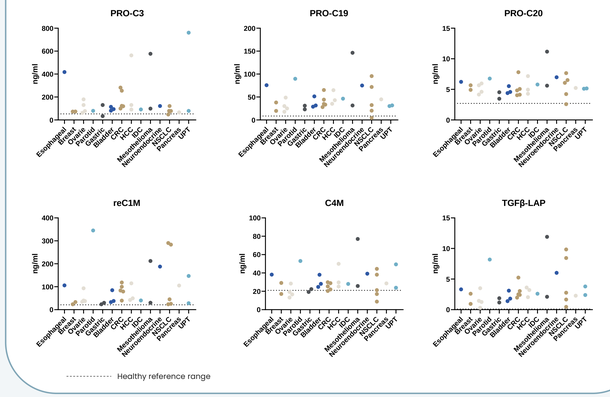
BIOMARKERS & RESULTS

Biology and Biomarker Overview

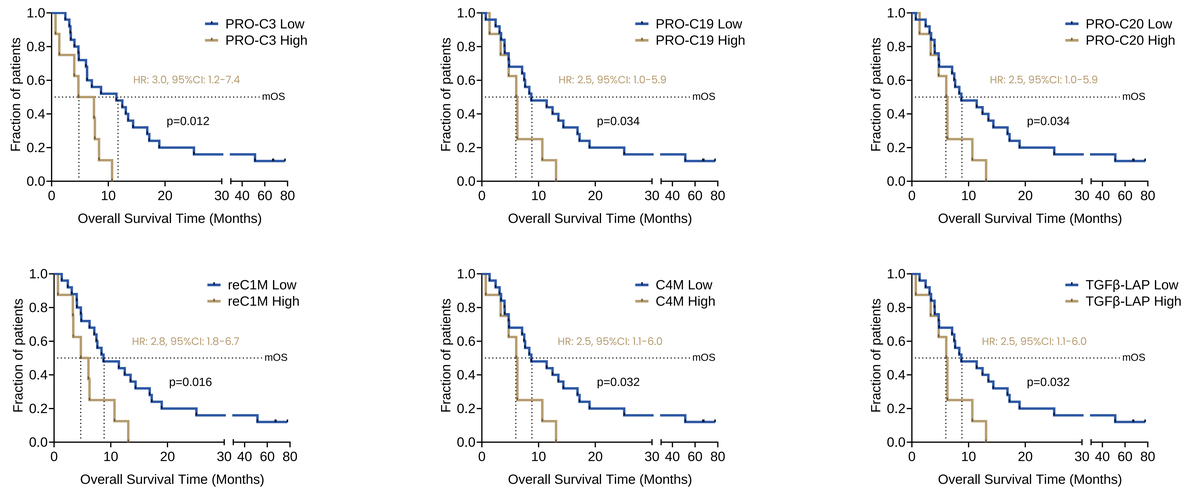


Biomarker	Description
PRO-C3	N-terminal pro-peptide of type III collagen
PRO-C19	C-terminus of type XIX collagen
PRO-C20	C-terminus of type XIX collagen
reC1M	A fragment of type I collagen released by MMP
C4M	A fragment of type IV collagen released by MMP
TGF-LAP	A fragment of LAP-TGF-b released by PLK

Scatter plots per indication



Non-invasive biomarkers associated with tumor fibrosis and collagen/ECM turnover identify cancer patients with poor prognosis



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