

# Progastrin, a Novel Ubiquitous Cancer Blood Biomarker for Early Detection and Monitoring

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## BACKGROUND AND HYPOTHESES

The successes of recent publications on "multi-tumor" circulating markers highlight the relevance of novel universal diagnostic cancer blood biomarkers. Since the Wnt/β-catenin/Tcf4 pathway, activated in many tumors, induces the *GAST* gene encoding progastrin, we hypothesized that progastrin, easily measurable in the blood, might be a "multi-tumor" diagnostic biomarker.

## METHODS

Progastrin levels were measured in the blood samples of 1267 patients with 11 different cancer origins, and compared to those of 557 asymptomatic 18-70 years old blood donors. Ovarian cancer samples were from CHIVA randomized phase II trial (NCT01583322, GINECO). Moreover the longitudinal kinetics of progastrin concentrations were serially assessed in 194 patients with peritoneal involvement from gastro-intestinal cancers enrolled in BIG-RENAPE trial (NCT03787056), and in 84 hepatocellular carcinoma (HCC) patients treated with different treatments. The progastrin was measured using an ELISA test developed by ECS progastrin (Prilly, Switzerland). For the statistical analysis, if not specified, unpaired t-test two-tailed was used.

## RESULTS: STUDY DEMOGRAPHICS

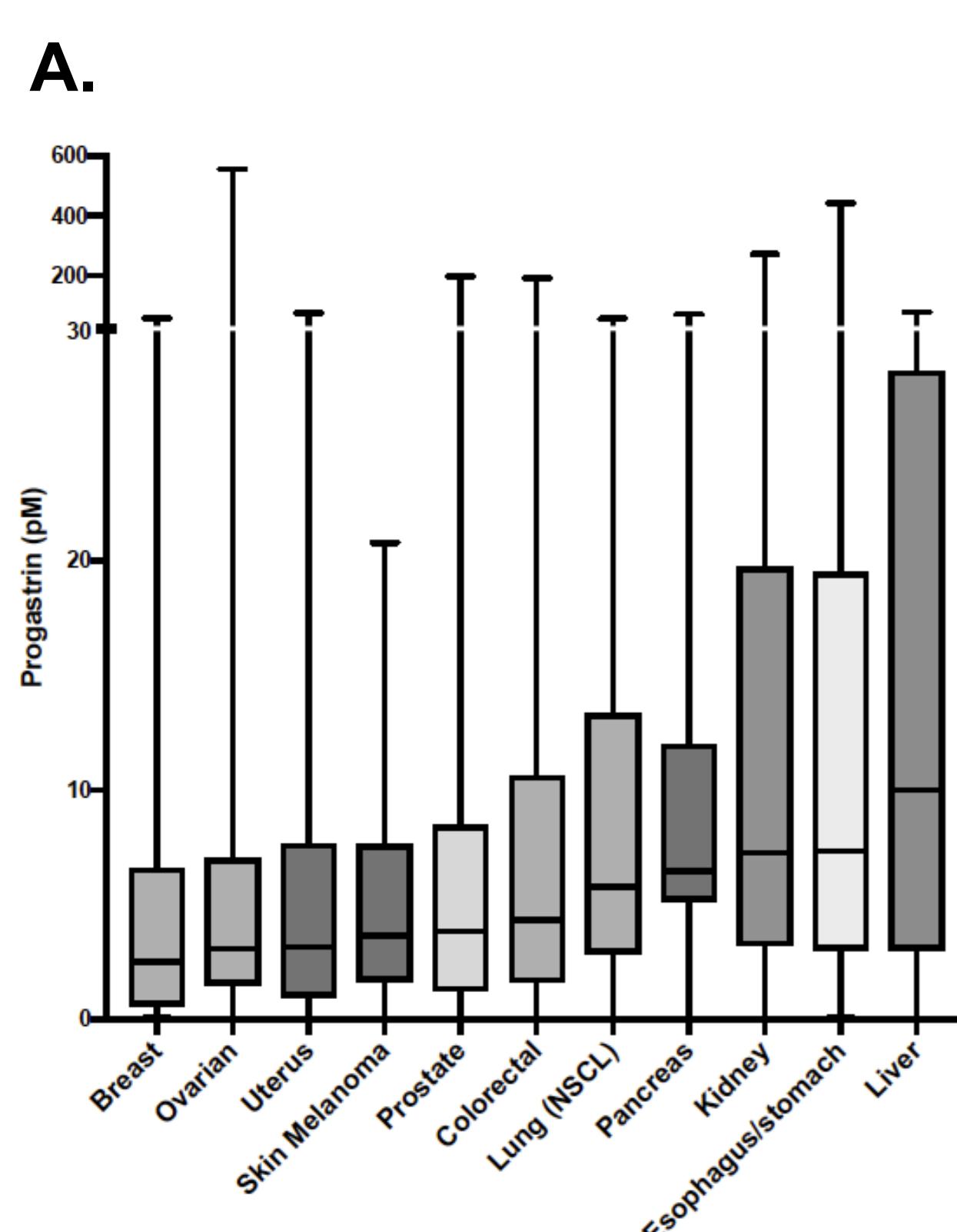
| Sample Status               | No. of Patients   | Gender* |        | Median Age (Years) (**) | Progastrin Median (IQR), pM | Progastrin Mean (SE), pM | AJCC Stage (number of Patients)***         |
|-----------------------------|-------------------|---------|--------|-------------------------|-----------------------------|--------------------------|--|
|                             |                   | Male    | Female |                         |                             |                          |  |
| All cancer                  | 1267              | 626     | 651    | 57 (23-93)              | 4.72 (1.83-11.76)           | 12.55 (0.89)             | II 318 III 243 IV 169 437                  |
| Breast                      | 62                | 0       | 62     | 57 (34-70)              | 3.93 (1.36-6.69)            | 6.34 (1.36)              | II 41 III 12 IV 6                          |
| CRC                         | 309               | 174     | 123    | 64 (23-83)              | 4.36 (1.62-10.59)           | 10.22 (1.92)             | Focal 25 Locally advanced 73 Metastatic 27 |
| Esophagus/stomach           | 72                | 29      | 43     | 65 (21-83)              | 7.41 (3.03-19.21)           | 21.72 (6.50)             | II 9 III 1 IV 7                            |
| Kidney                      | 184               | 135     | 48     | 64 (25-85)              | 7.25 (3.22-19.66)           | 21.50 (2.96)             | II 5 III 19 IV 15 144                      |
| Liver                       | 95                | 78      | 17     | 67 (23-86)              | 9.99 (3.03-28.28)           | 17.21 (1.91)             | II 2 III 25 IV 42 22                       |
| Lung (NSCLC)                | 60                | 39      | 21     | 67 (45-85)              | 5.78 (2.93-13.15)           | 10.39 (1.57)             | II 30 III 21 IV 8 1                        |
| Skin Melanoma               | 38                | 0       | 38     | 61 (38-79)              | 3.65 (1.65-7.44)            | 5.09 (0.79)              | II 0 III 0 IV 0 33                         |
| Ovary                       | 211               | 0       | 211    | 62 (22-86)              | 3.11 (1.11-11.29)           | 10.32 (2.71)             | II 21 III 7 IV 142 39                      |
| Pancreas                    | 54                | 17      | 37     | 66 (50-89)              | 6.47 (4.02-11.89)           | 11.72 (2.80)             | II 13 III 17 IV 3 1                        |
| Prostate                    | 134               | 134     | 0      | 66 (46-90)              | 3.65 (1.25-8.36)            | 9.87 (2.06)              | II 0 III 12 IV 50 72                       |
| Uterus (endometrium/cervix) | 68                | 0       | 68     | 60 (29-90)              | 3.13 (0.99-7.58)            | 7.27 (1.52)              | II 40 III 21 IV 4 2                        |
| Healthy blood donors        | No. of Volunteers | Male    | Female | Median Age, Years       | Progastrin Median (IQR), pM | Progastrin Mean (SE), pM |  |
| All donors                  | 557               | 310     | 247    | 35 (18-70)              | 1.05 (0.00-2.92)            | 2.04 (0.11)              |  |
| 18-25 years old             | 137               | 79      | 58     | 22                      | 0.2 (0.00-1.07)             | 0.99 (0.16)              |  |
| 18-29 years old             | 213               | 117     | 96     | 24                      | 0.43 (0.15)                 | 1.23 (0.14)              |  |
| 30-39 years old             | 123               | 69      | 54     | 35                      | 1.06 (0.12-2.3)             | 1.85 (0.20)              |  |
| 40-70 years old             | 221               | 124     | 97     | 50                      | 1.85 (0.5-4.0)              | 2.90 (0.21)              |  |

\* 38 missing gender (3.0%)

\*\* 53 undetermined age (4.18%)

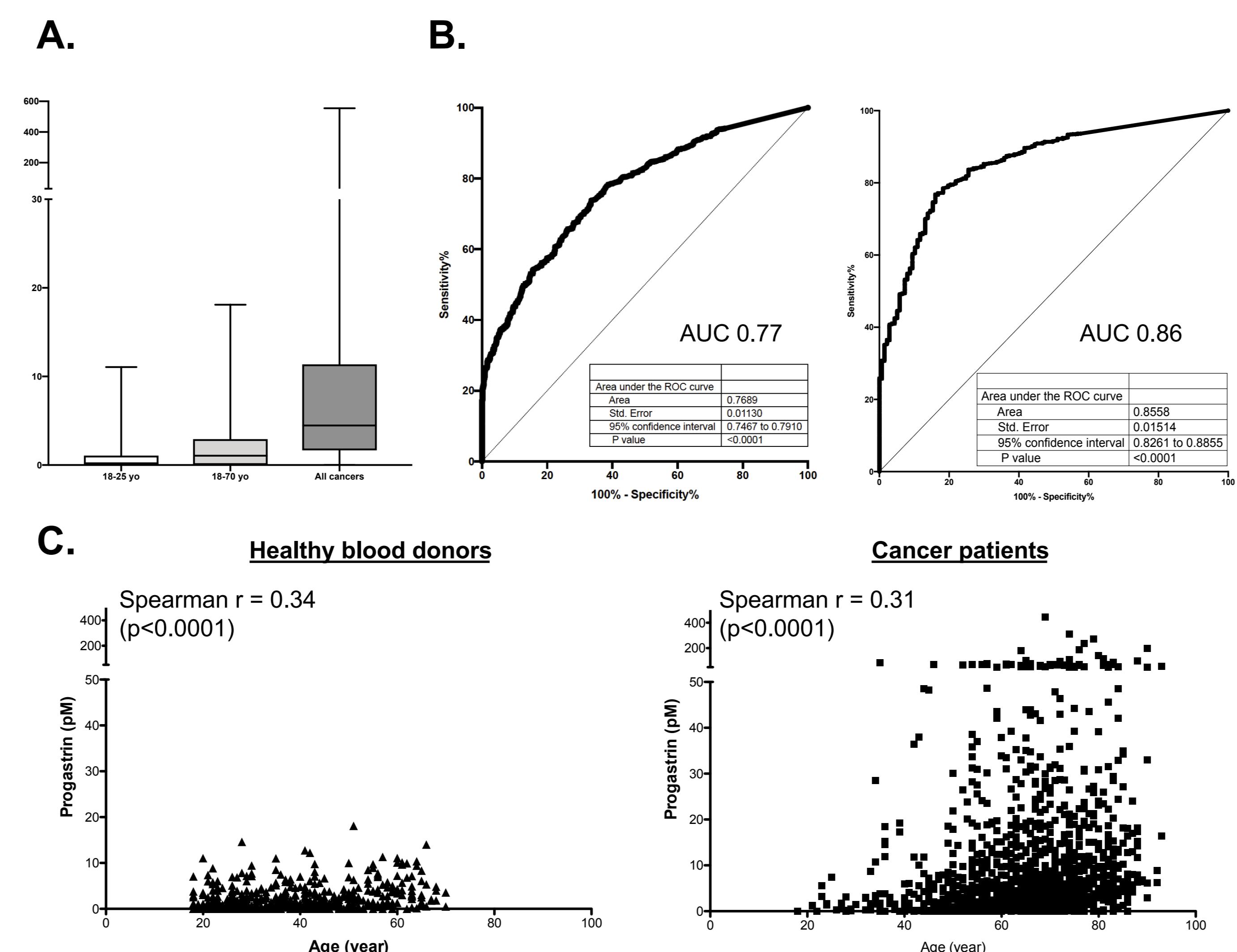
\*\*\* 40 undetermined stage (3.15%)

## ELEVATED PROGASTRIN LEVELS IN CANCER PATIENTS REGARDLESS OF DISEASE STAGES



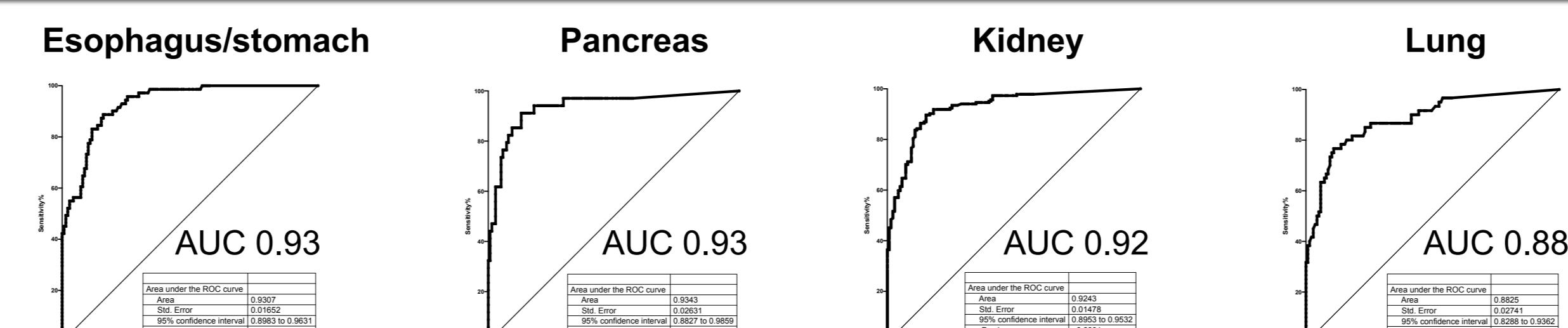
A. Progastrin concentrations in patients with cancer from 11 different origins. All subtypes combined, the median progastrin concentration was 4.72pM (interquartile range, (IQR): 1.83-11.76pM) B. Baseline median progastrin concentrations according to disease stages.

## PROGASTRIN LEVELS IN HEALTHY BLOOD DONORS COMPARED TO CANCER PATIENTS



A. Progastrin concentrations in 18-70 yo and 18-25 yo healthy blood donors compared to those in all combined cancers. B. Diagnostic discriminative accuracy of progastrin in all cancer patients compared to 18-70 yo and 18-25 yo healthy blood donors using Receiver Operating Characteristics (ROC) curve analysis. C. Correlation between progastrin concentrations and age in healthy blood donors and cancer patients.

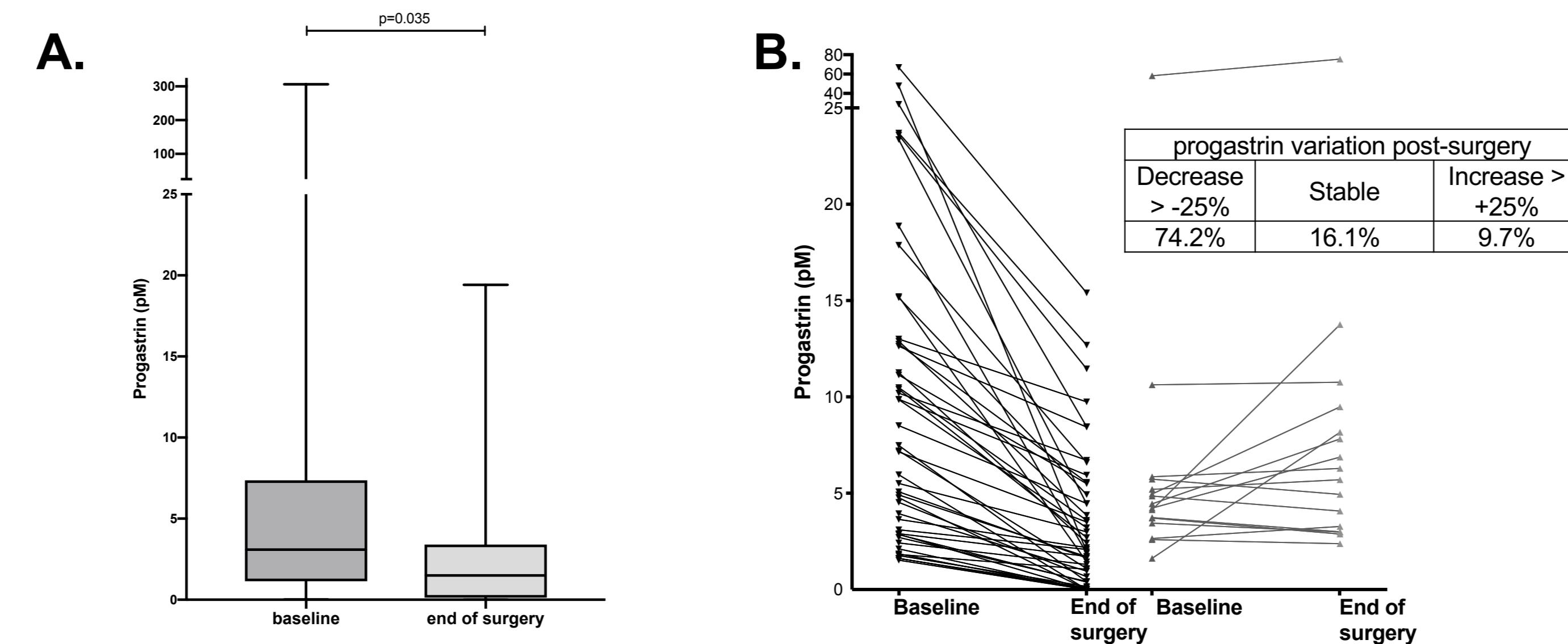
## DIAGNOSTIC ACCURACIES OF PROGASTRIN IN 4 CANCERS



Diagnostic discriminative accuracy of progastrin in 4 cancer patients compared to 18-25 years old healthy blood donors.

## PROGASTRIN IS A BIOMARKER FOR PATIENT FOLLOW-UP

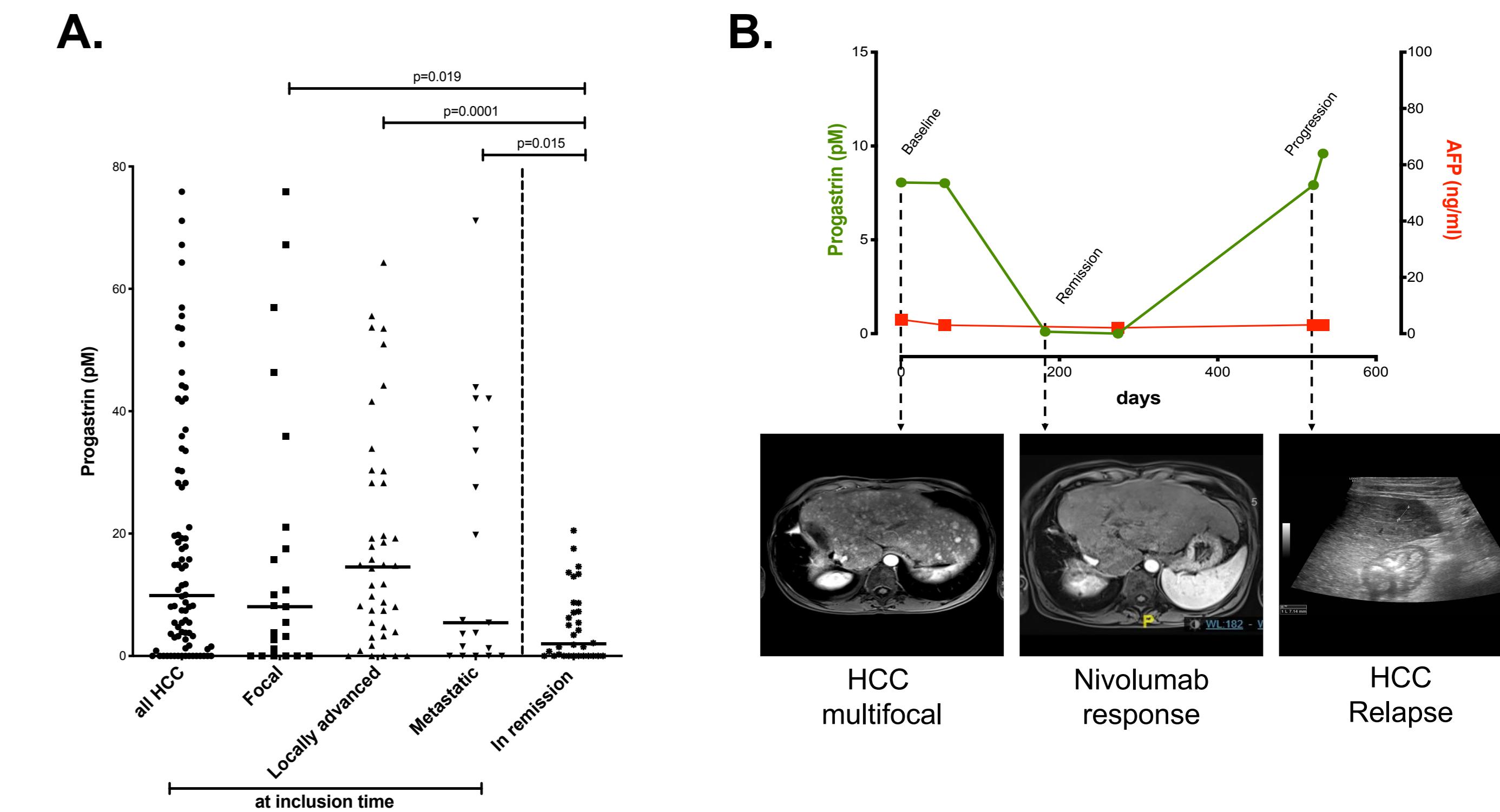
### 1. PRO-RENAPE cohort



A. Changes in median progastrin concentrations from baseline (n=194) to post-operative time (n=85) in patients with peritoneal carcinomatosis from gastrointestinal cancers treated with or without peri-operative chemotherapy. B. Progastrin changes at individual levels (n=62).

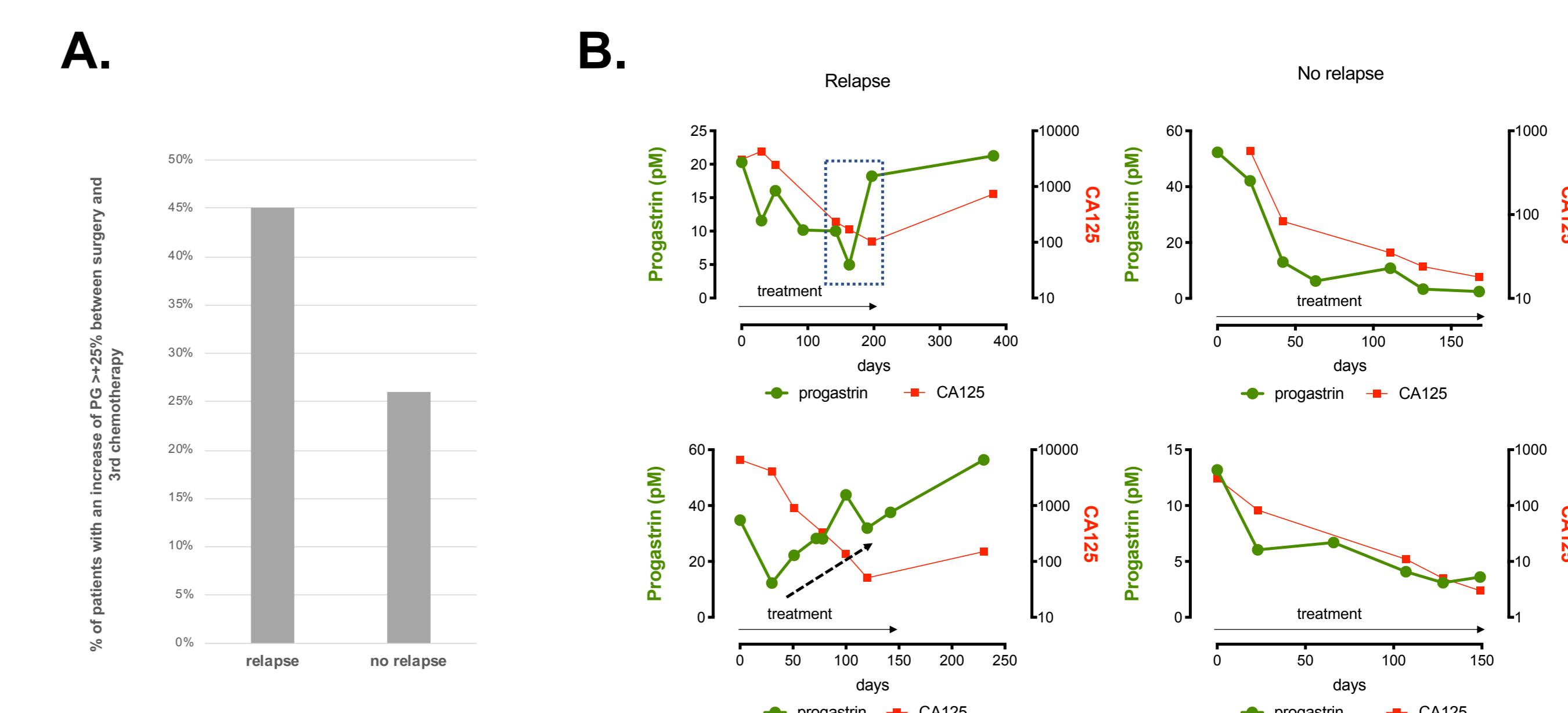
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### 2. PRO- HCC cohort



A. Progastrin levels at different disease stages (focal, n=23; locally advanced, n=42; metastatic disease, n=19) and at disease remission after treatment (n=32). B. Progastrin longitudinal changes during the disease treatment management steps (baseline, remission, progression) with consistent imaging findings at the same times in a typical patient.

### 3. PRO-CHIVA cohort



A. Percentage of patients with progastrin increase > 25% between surgery and third post-operative chemotherapy cycle, according to relapse occurrences (yes vs no), with a 1.2 year follow-up (n=188). B. Progastrin and CA-125 longitudinal kinetics in 4 typical patients.

## ONGOING VALIDATION PROSPECTIVE STUDIES

**ONCOPRO:** Validation of the diagnostic and monitoring values of progastrin in 16 different types of cancers managed with curative or palliative intent treatments (NCT03787056).

**PROCODE:** Validation of the screening value of progastrin in colorectal cancers (NCT03775473).

## CONCLUSIONS

- Progastrin is a novel ubiquitous cancer biomarker.
- Progastrin is easily detectable in the blood using an affordable ELISA test (CancerRead Lab test®).
- Progastrin may change the current paradigms for cancer screening, diagnostic and monitoring.