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Introduction

- Non-small cell lung cancer (NSCLC) is a prevalent and lethal malignancy. Early diagnosis and monitoring of disease progression are crucial for enhancing patient outcomes. Current approaches, including imaging and tumor marker analysis such as cytokeratin-19 fragment 21-1 (CYFRA 21-1) carcinoembryonic antigen (CEA) and carbohydrate antigen 125 (CA-125), often exhibit sensitivity and specificity limitations.

- Progastrin, an 80-amino acid intracellular precursor of the gastrin hormone encoded by the *GAST* gene, primarily regulates acid secretion. Pathological *GAST* overexpression leads to protein accumulation and release of Circulating Progastrin (hPG₈₀), detectable in the blood of cancer patients.

- The goal of this study is to investigate the role of this novel marker in NSCLC.

Objectives

- To determine the hPG₈₀ concentration of patients with NSCLC at the time of diagnosis.
- To compare hPG₈₀ with other commonly used blood-based biomarkers for the diagnosis and monitoring of NSCLC.

Methods

- Prior to treatment, blood samples were collected from all participants using EDTA-containing tubes. Plasma was isolated and stored at -80°C until further analysis.

- The concentration of hPG₈₀ was determined using the ELISA DxPG₈₀ lab kit (BIODENA CARE, France) according to manufacturer's guidelines.

- Patients were categorized by therapeutic approach into curative and palliative groups:

- Potentially curative therapy:** Surgery with adjuvant and/or neoadjuvant chemotherapy (CT) with or without immunotherapy (IO) or targeted therapy, or radical treatment (sequential or concurrent CT and radiation therapy with or without IO).

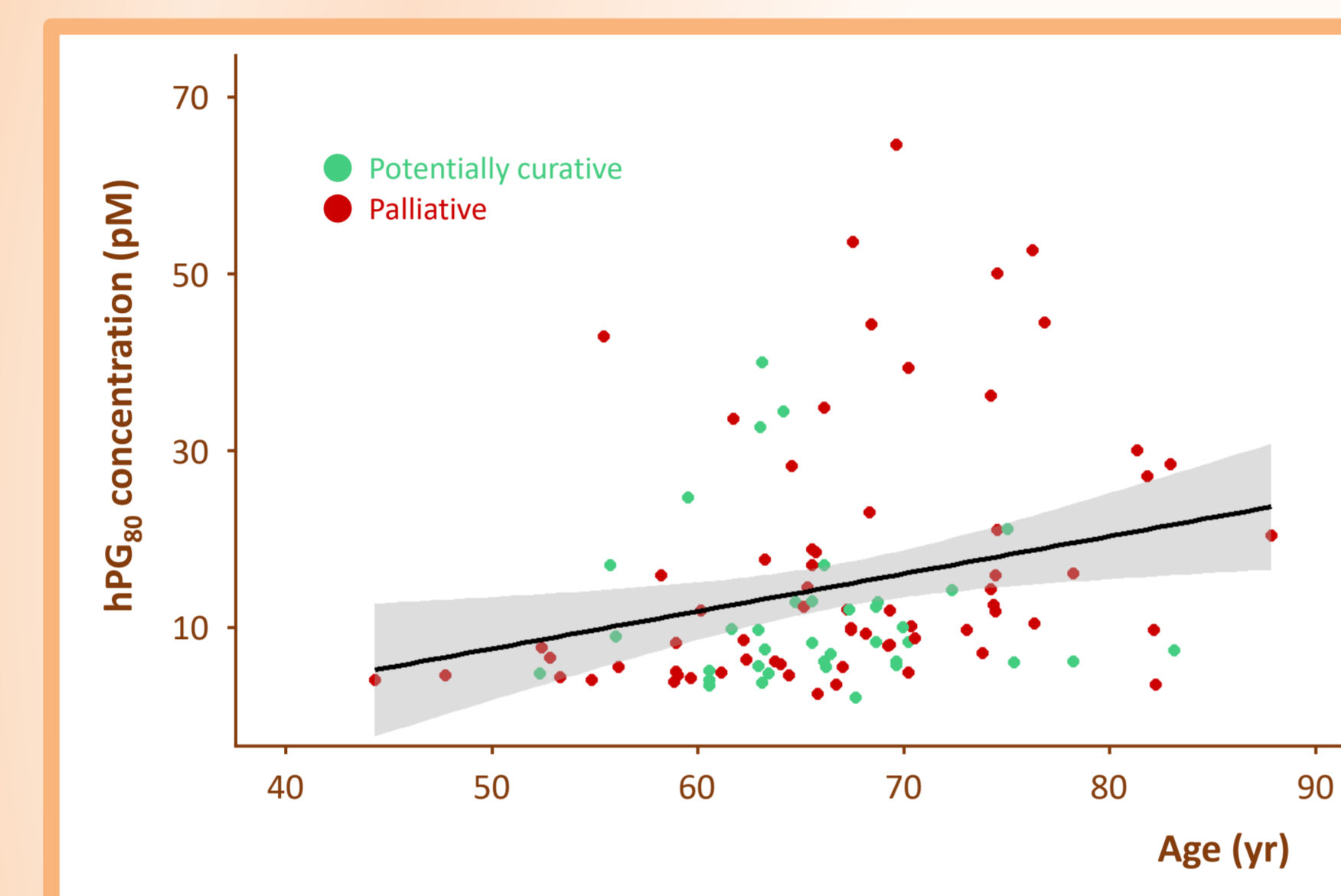
- Palliative therapy:** Systemic approaches: CT, IO, CT combined with IO and targeted agents.

Results

Patients

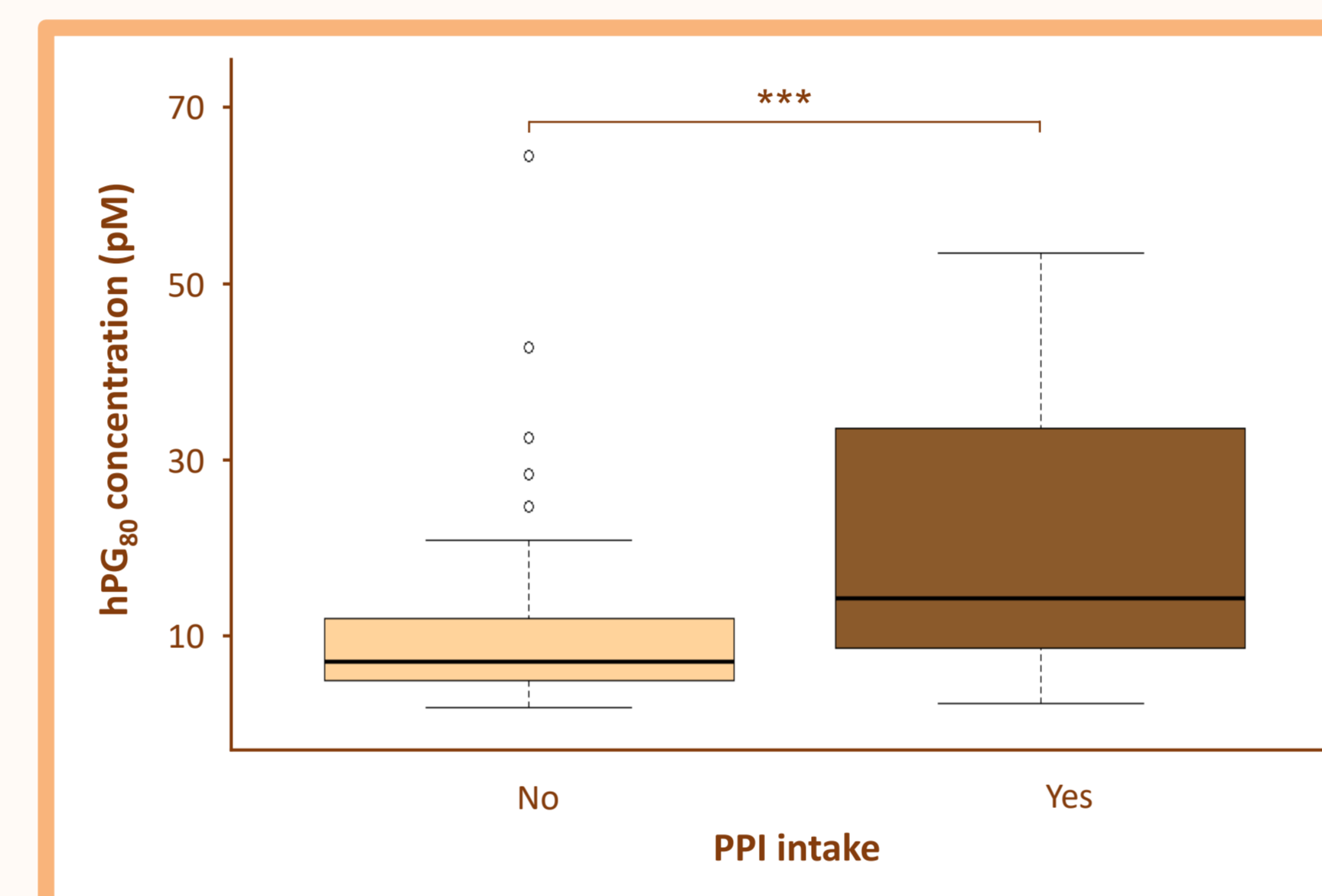
This prospective study included 105 NSCLC patients (56 females, 49 males) with a mean age of 66.7 ± 7.8 years in stage I-II (8.6%), III (31.4%) and IV (60%)

hPG₈₀ and age



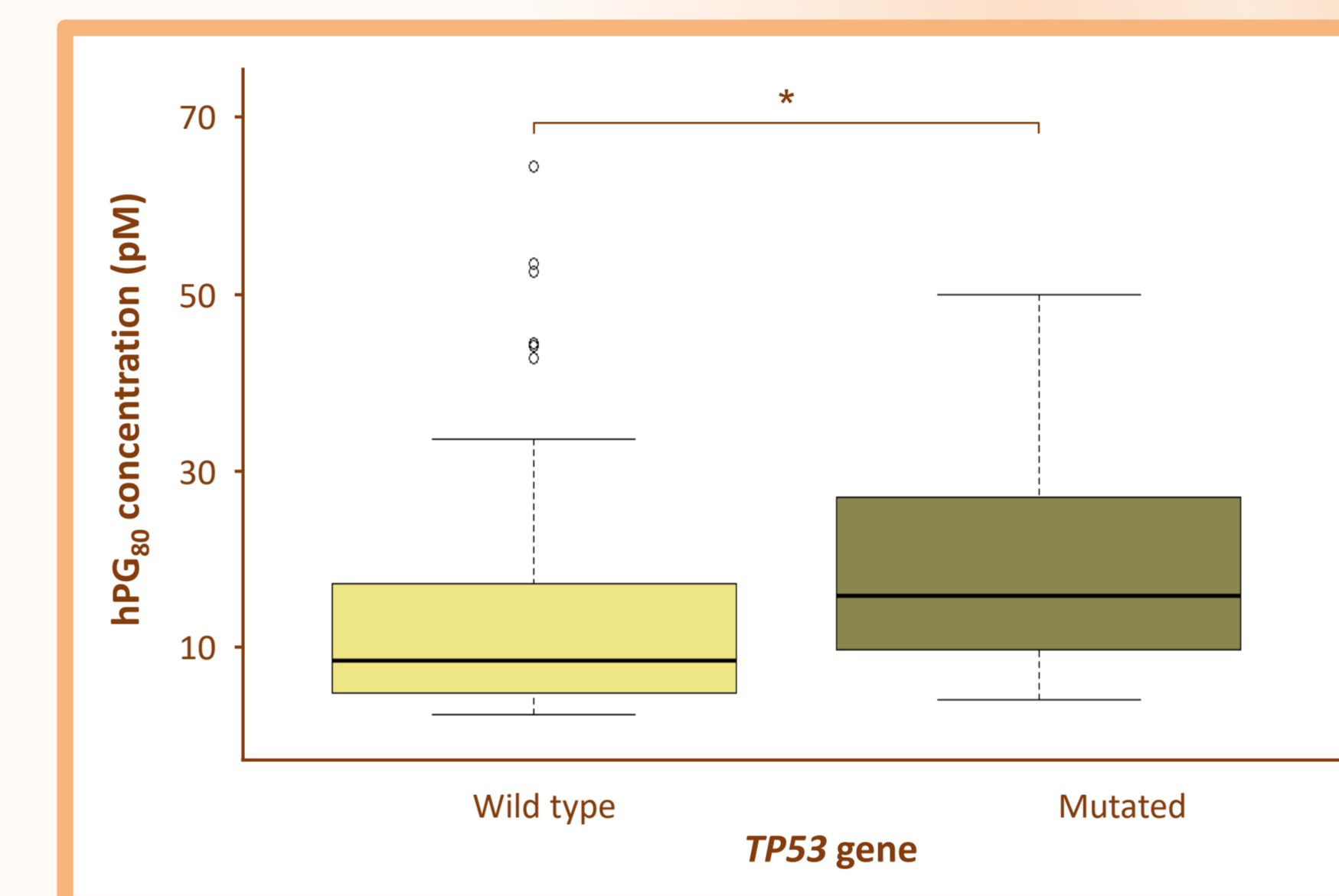
Spearman's rank correlation coefficient showed a significant positive correlation between hPG₈₀ expression levels and age in the NSCLC patient cohort ($r = 0.34$, $p < 0.001$).

hPG₈₀ levels and PPI intake



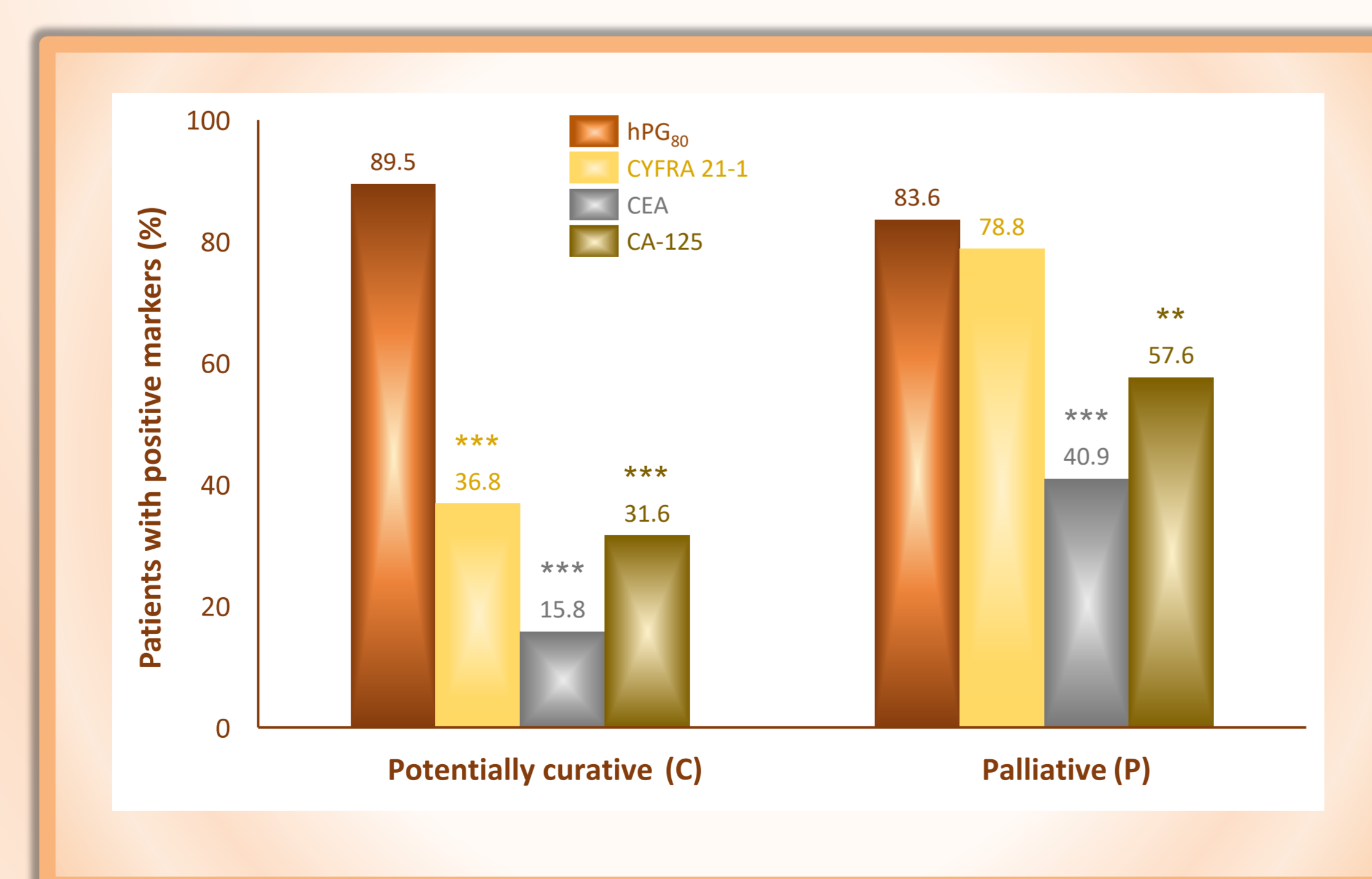
Proton pump inhibitor (PPI) administration and its impact on plasma hPG₈₀ concentration. PPI-treated patients had substantially increased hPG₈₀ levels compared to the non-PPI group. ***($p < 0.001$)

hPG₈₀ expression and TP53 mutations

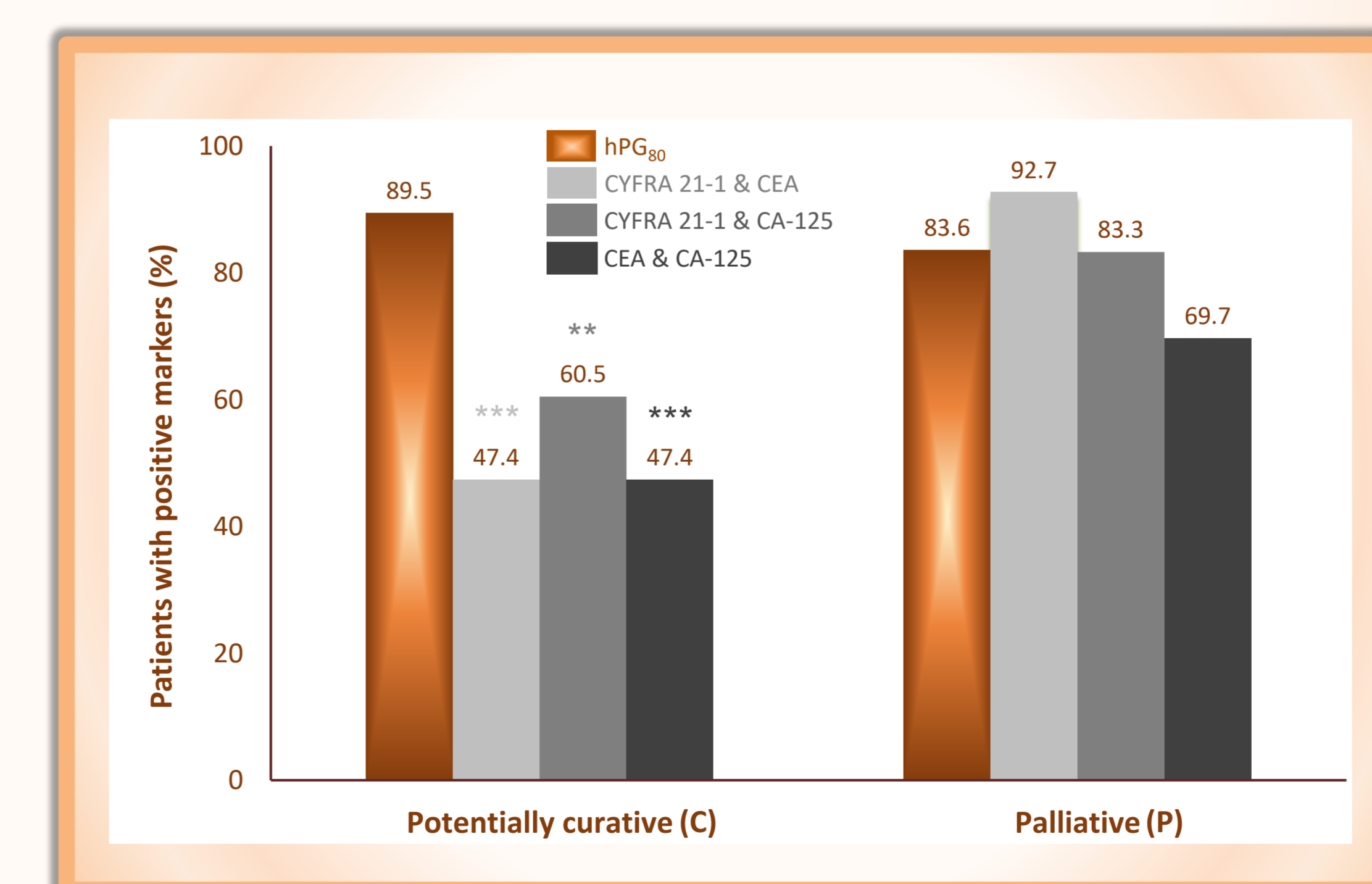


Effect of *TP53* genotype on hPG₈₀ levels. Patients carrying *TP53* mutations showed a statistically significant increase in hPG₈₀ expression compared to patients with the wild-type genotype. *($p < 0.05$).

hPG₈₀ and current blood-based tumor markers in NSCLC



Proportion of patients exhibiting positive expression of each marker in the disease cohort undergoing curative therapy (C) and the advanced-stage disease group receiving palliative therapy (P). hPG₈₀ was elevated in nearly 90% of cohort C, exceeding the positivity rate of other biomarkers (CYFRA 21-1, CEA and CA-125), which remained below 40%. In cohort P, hPG₈₀ positivity was comparable to CYFRA 21-1, both demonstrating higher positivity rates than CEA and CA-125. ***($p < 0.001$); **($p < 0.01$).



Diagnostic performance of hPG₈₀ and paired blood-based markers in curative (C) and palliative (P) therapy groups. In the C cohort, hPG₈₀ demonstrated significantly higher accuracy than all other combinations. In the P cohort, the three marker set assays were comparable, but not statistically superior to hPG₈₀ alone. The hPG₈₀/CYFRA 21-1 marker pair did not improve accuracy over hPG₈₀ independently (data not shown). ***($p < 0.001$); **($p < 0.01$).

Conclusions

- The present study highlights the enhanced diagnostic and prognostic capabilities of the hPG₈₀ in NSCLC, particularly in early or locally-advanced disease where conventional blood-based tumor markers exhibit limited sensitivity.

- A prolonged follow-up period is necessary to evaluate the consistency and robustness of the findings and their role in monitoring disease.

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Conflict-of-interest statement

The author of this poster has no conflicts of interest to declare.

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