

Early modulation of pituitary gonadotropins during PD-1 inhibitor–based immunochemotherapy in patients with solid tumors

Deyu Yang

Guangzhou University of Chinese Medicine

Xinrong Chen

Guangzhou University of Chinese Medicine

Zhichao Li

Guangzhou University of Chinese Medicine

Mei Ouyang

Guangzhou University of Chinese Medicine

Ke Wang

Guangzhou University of Chinese Medicine

Chuangjie Zheng

Guangzhou University of Chinese Medicine

Linzhu Zhai

linzhuzhai@gzucm.edu.cn

First Affiliated Hospital of Guangzhou University of Chinese Medicine

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Abstract

Lung cancer and colorectal cancer are among the most frequently diagnosed malignancies worldwide, with their systemic management increasingly incorporating combinations of chemotherapy and immune checkpoint blockade. However, how these treatment strategies affect endocrine regulation during therapy remains poorly characterized. This longitudinal observational study investigated alterations in circulating sex hormones in patients with lung cancer and colorectal cancer receiving PD-1 inhibitor–based immunochemotherapy. Serum levels of pituitary-derived hormones, including luteinizing hormone (LH), follicle-stimulating hormone (FSH), the LH/FSH ratio, and prolactin (PRL), along with those of gonadal sex steroids, such as testosterone, estradiol, and progesterone, were measured at baseline and at predefined serial time points throughout treatment. Pituitary hormone dynamics exhibited distinct temporal patterns during therapy. FSH showed significant longitudinal variation that increased progressively over time, while LH displayed a more modest upward trend that reached statistical significance only at later follow-up. In parallel, the LH/FSH ratio declined during treatment, while PRL levels increased significantly. In contrast, circulating gonadal sex steroids—including testosterone, estradiol, and progesterone—showed no significant longitudinal changes at the cohort level. These findings indicate that PD-1 inhibitor–based immunochemotherapy is associated with selective early changes in pituitary-derived hormones, while gonadal sex steroids remain comparatively stable, supporting a predominantly pituitary-level endocrine response rather than overt gonadal dysfunction.

INTRODUCTION

As among the most commonly diagnosed malignancies worldwide, lung and colorectal cancers remain major causes of cancer-related mortality^[1]. In recent years, the combination of immune checkpoint inhibitors with chemotherapy has significantly influenced the treatment landscape of multiple solid tumors, particularly advanced non-small-cell lung cancer^[2]. Blockade of the programmed cell death protein 1 (PD-1) pathway has shown clinical efficacy across multiple tumor types and treatment settings^[3]. Hence, the immunochemotherapy-based approach represents a common contemporary systemic treatment strategy.

In addition to their antitumor effects, systemic cancer therapies may exert broader biological influences, such as the modulation of endocrine regulation^[3]. It has long been recognized that chemotherapy impairs gonadal function through direct cytotoxic effects and, in some treatment settings, may also facilitate dysregulation of hypothalamic–pituitary signaling^[4, 5]. With immune responses being closely intertwined with endocrine signaling pathways, the addition of immune checkpoint inhibition introduces further biological complexity^[6]. Sex hormones influence both innate and adaptive immunity^[7], and potential sex-related differences in outcomes following immunotherapy have been reported in several tumor types^[8]. Nevertheless, current evidence remains inconsistent, with most studies focusing on biological sex rather than dynamic hormonal changes during treatment.

Pituitary-derived hormones, including luteinizing hormone (LH), follicle-stimulating hormone (FSH), and prolactin (PRL)^[9], along with gonadal sex steroids, constitute key components of the hypothalamic–pituitary–gonadal (HPG) axis and are closely related to immune regulation^[10]. Their biological relevance notwithstanding, longitudinal data describing hormone dynamics during combined chemotherapy and PD-1 blockade remain scarce, particularly during early treatment cycles. Therefore, aiming to characterize early endocrine modulation associated with contemporary systemic cancer treatment, retrospective observational study examined serial changes in pituitary and gonadal hormones in patients with lung cancer and colorectal cancer receiving PD-1 inhibitor–based immunochemotherapy.

Patients and methods

Study populations and data collection

A retrospective observational study was conducted in patients with lung cancer and colorectal cancer who had received immunochemotherapy at our institution between May 2021 and June 2025. All patients were treated with PD-1 inhibitors combined with chemotherapy according to routine clinical practice. The study was approved by the Ethics Committee of the First Affiliated Hospital of Guangzhou University of Chinese Medicine. All procedures were conducted in accordance with the Declaration of Helsinki and relevant guidelines and regulations.

A fixed-dose regimen of PD-1 inhibitors was administered intravenously every three weeks in accordance with approved prescribing information. The selection of chemotherapy regimens was based on tumor type and clinical indication, including taxane- or platinum-based regimens for lung cancer and capecitabine-based regimens, with or without oxaliplatin, for colorectal cancer. Treatment was delivered in repeated cycles, with hormone assessments conducted in accordance with the treatment schedule.

Clinical data—including demographic characteristics, tumor type, treatment regimen, and treatment cycle information—were obtained from electronic medical records. Quantitative serum measurements of FSH, LH, PRL, testosterone, estradiol (E2), and progesterone were performed at predefined clinical time points. Hormone levels were measured at baseline prior to treatment initiation (week 0), and after the first (week 3), second (week 6), and third (week 9) treatment cycles. According to their medical history, all female patients included in the analysis were postmenopausal and were not receiving hormone replacement therapy during the study period.

Statistical analysis

Statistical analyses were performed using SPSS 26.0 (IBM Corp., Chicago, IL, USA). Figures and graphical representations were generated using GraphPad Prism 8.4.1 (GraphPad Software, San Diego, CA, USA). Continuous variables are presented as median (interquartile range, IQR) or mean $\pm$ standard deviation, as appropriate, while categorical variables are summarized as frequencies and percentages.

Results

Baseline characteristics

Baseline data were obtained for a total of 34 patients with solid tumors who had received PD-1 inhibitor–based immunochemotherapy between May 2021 and June 2025. The cohort, comprising 24 men and 10 women, included 23 patients with lung cancer and 11 patients with colorectal cancer.

The median age of the overall study population was 55 years. Among patients with lung cancer, the median age was 63.5 years, while among those with colorectal cancer, it was 52 years. All of the patients received PD-1 inhibitor–based immunochemotherapy, with chemotherapy regimens selected according to tumor type. Table 1 summarizes the baseline hormone levels of the overall cohort.

Table 1
Baseline hormone levels. Data are presented as median (interquartile range, IQR). Baseline values were defined as measurements obtained at TIME = 0.

Hormone	Overall (n = 34)	LC (n = 23)	CRC (n = 11)
FSH	12.97 (7.27–30.44)	12.41 (7.43–23.54)	19.90 (8.56–41.12)
LH	10.13 (7.23–18.23)	8.57 (7.08–17.10)	13.79 (8.97–26.95)
LH/FSH	0.81 (0.61–1.19)	0.84 (0.58–1.22)	0.75 (0.67–1.04)
PRL	327.00(226.27-449.23)	277.10(201.95–347.65)	448.40(317.00–600.05)
Testosterone	8.81 (1.08–17.04)	8.82 (3.47–16.08)	8.79 (0.49–17.46)
Estradiol	104.80(71.95–154.80)	107.00(85.42–149.15)	96.68 (38.83–160.80)
Progesterone	0.65 (0.38–0.94)	0.64 (0.32–0.92)	0.66 (0.52–0.97)

Overall longitudinal changes in pituitary gonadotropins during immunochemotherapy

In the overall cohort (n = 34), FSH levels increased in a time-dependent manner during treatment, rising from a baseline median of 12.96 (IQR 7.27–30.44) to 17.18 (12.49–31.11) at 3 weeks, 22.21 (15.04–38.80) at 6 weeks, and 24.36 (17.76–49.49) at 9 weeks. While the increase at 3 weeks did not achieve statistical significance, FSH levels were significantly higher at 6 weeks (adjusted p = 0.0002), further increasing at 9 weeks (adjusted p < 0.0001) compared with baseline. In contrast, LH demonstrated a modest temporal pattern, with median levels of 10.13 (7.23–18.23) at baseline, 13.51 (8.91–18.25) at 3 weeks, 13.52 (9.36–20.41) at 6 weeks, and 14.44 (11.02–25.32) at 9 weeks. No significant differences were observed at 3 or 6 weeks; however, LH levels were significantly higher at 9 weeks than at baseline (adjusted p = 0.0042) (Fig. 1).

Cancer-specific hormone characteristics

In the lung cancer cohort (n = 23), FSH levels increased progressively over time, rising from a baseline median of 12.41 (IQR 7.43–23.54) to 21.29 (17.10–38.60) at 9 weeks (adjusted p < 0.0001); however, no significant differences were observed at 3 weeks [16.21 (9.94–30.60)] or 6 weeks [16.10 (13.80–32.42)] compared with baseline. LH demonstrated a modest upward trend, with median values increasing from 8.57 (7.08–17.10) at baseline to 13.86 (10.24–22.17) at 9 weeks; however, none of the pairwise comparisons achieved statistical significance. Conversely, the LH/FSH ratio declined progressively from 0.836 (0.578–1.224) at baseline to 0.576 (0.460–0.821) at 6 weeks and 0.597 (0.529–0.695) at 9 weeks, with significant reductions at both time points (adjusted p = 0.0494 and 0.0129, respectively). PRL levels were elevated during follow-up, rising from a baseline median of 277.10 (201.95–347.65) to 441.60 (339.85–585.95) at 6 weeks and 557.10 (419.15–806.76) at 9 weeks (adjusted p = 0.0003 and < 0.0001, respectively) (Fig. 2).

By comparison, serum testosterone, E2, and progesterone levels demonstrated stability over time. Median (IQR) values were as follows: for testosterone, 8.82 (3.46–16.08) at baseline and 13.49 (1.88–19.92) at 9 weeks; for E2, 107.00 (85.42–149.15) and 91.39 (66.76–151.40); and for progesterone, 0.64 (0.32–0.92) and 0.65 (0.34–0.85). No statistically significant longitudinal differences were observed.

Patients with colorectal cancer (n = 11) exhibited generally modest endocrine changes during treatment. FSH levels rose from a baseline median of 19.90 (IQR 8.56–41.12) to 22.95 (14.08–38.91) at 3 weeks, 30.75 (21.88–50.88) at 6 weeks, and 35.50 (24.15–54.88) at 9 weeks. A significant increase was observed at 3 weeks compared with baseline (p = 0.032). On the contrary, no significant longitudinal change was observed in LH levels, with median values of 13.79 (8.97–26.95), 15.58 (10.45–26.40), 17.74 (13.57–24.84), and 22.79 (14.65–27.68) at baseline, 3, 6, and 9 weeks, respectively. Over time, PRL levels remained relatively stable, with median values of 448.40 (317.00–600.05) at baseline, 484.00 (362.60–554.60) at 3 weeks, 427.80 (360.60–523.15) at 6 weeks, and 428.00 (386.05–557.50) at 9 weeks. Similarly, testosterone, E2, and progesterone levels showed no significant longitudinal changes during follow-up (Fig. 2).

Sex-specific hormone characteristics

In male patients (n = 24), the median FSH level increased from 10.71 (IQR 6.97–16.95) at baseline to 15.44 (11.13–23.19) at week 3; however, this early change was not statistically significant (adjusted p = 0.3526). FSH levels continued to rise during follow-up, becoming significantly higher at 6 weeks (adjusted p = 0.0010) and 9 weeks (adjusted p < 0.0001) than at baseline. LH showed a comparable upward trend, rising from 8.07 (6.34–13.26) to 10.55 (7.55–14.61) at week 3 without statistical significance (adjusted p = 0.6563); however, significant increases were observed at 6 weeks (adjusted p = 0.0304) and 9 weeks (adjusted p = 0.0004). PRL levels also increased from 267.55 (176.22–365.50) at baseline to 365.90 (277.43–478.45) at week 3, although the difference was not significant (adjusted p = 0.1009). Subsequent increases were significant at both 6 weeks (adjusted p = 0.0007) and 9 weeks (adjusted p < 0.0001). In contrast, E2 levels decreased modestly from 125.50 (97.50–158.75) to 106.60 (92.44–130.68), while testosterone and progesterone remained relatively stable over the same period

(testosterone: 15.07 [8.79–18.08] vs. 15.86 [7.48–20.29]; progesterone: 0.66 [0.51–0.93] vs. 0.77 [0.46–0.94]). No statistically significant longitudinal changes were observed for these hormones.

In female patients (n = 10), baseline FSH levels were higher than those in male patients and remained similar at week 3 (52.47 [13.75–57.70] vs. 52.67 [25.12–59.48]; adjusted p > 0.9999). No significant change was detected at 6 weeks (adjusted p = 0.1702), whereas at 9 weeks, FSH levels were significantly elevated compared with baseline (adjusted p = 0.0097). Levels of LH, PRL, E2, testosterone, and progesterone fluctuated minimally over time, showing no statistically significant longitudinal changes (Fig. 3).

Discussion

During PD-1 inhibitor–based immunochemotherapy, longitudinal endocrine monitoring in the overall cohort demonstrated progressive changes predominantly at the level of pituitary hormones. FSH levels increased over time, with statistically significant elevations observed at later follow-up time points compared with baseline. In contrast, LH increased gradually, reaching statistical significance only at the later stage of follow-up. Supporting these findings, the LH/FSH ratio declined during treatment, indicating that the relative increase in FSH levels was greater than that in LH levels. Rather than signifying a uniform activation of the HPG axis, this pattern marks a shift in the balance of pituitary gonadotropin secretion.

Importantly, these alterations occurred without parallel, sustained changes in circulating gonadal sex steroids, such as testosterone, E2, and progesterone. This dissociation between pituitary gonadotropins and peripheral sex steroids suggests that endocrine modulation during immunochemotherapy may primarily involve central regulatory mechanisms, rather than overt gonadal failure. FSH, a widely regarded sensitive indicator of perturbations within the HPG axis, may reflect subtle changes in gonadal feedback or stress-related neuroendocrine regulation^[11, 12]. Previous studies on the endocrine system have shown that elevations in FSH levels may serve as an early marker of gonadal dysfunction, even before clinically overt hypogonadism becomes apparent^[13], reflecting adaptive pituitary responses rather than irreversible gonadal damage.

The hormonal pattern observed in our cohort is distinct from the classical endocrine profile of cytotoxic chemotherapy–induced hypogonadism and suggests that PD-1-based immunotherapy may predominantly modulate pituitary function rather than cause overt gonadal failure. Emerging evidence shows that systemic immune activation and inflammatory signaling can alter neuroendocrine function, including pituitary hormone secretion, independent of direct gonadal injury^[14]. Within this context, the early elevation in pituitary gonadotropins observed during combined chemotherapy and PD-1 blockade may reflect central neuroendocrine sensitivity to treatment-related immune and metabolic stress rather than permanent endocrine dysfunction.

In the present study, a distinct pattern of endocrine modulation was observed during PD-1 inhibitor–based immunochemotherapy, particularly in the lung cancer subgroup. Relative to the classical endocrine toxicity typically described after cytotoxic chemotherapy alone, early alterations in pituitary gonadotropins were modest, while PRL exhibited the most noticeable longitudinal change in this population. Specifically, PRL levels did not increase significantly after the initial treatment cycle but demonstrated a marked and statistically significant elevation at later follow-up time points, suggesting a delayed and progressive response, as opposed to an acute stress-related fluctuation. This temporal pattern signifies that the observed increase in PRL levels is unlikely to be explained solely by transient treatment-associated stress. Rather, it may reflect cumulative neuroendocrine–immune interactions that develop during sustained PD-1 blockade^[15]. Of note, the longitudinal increase in PRL occurred alongside only modest changes in pituitary gonadotropins and without significant declines in circulating sex steroids. These findings underline the possibility that PRL regulation during immunochemotherapy may be partially independent of classical HPG axis dynamics.

To the best of our knowledge, no prior study has systematically characterized delayed PRL elevation during PD-1 inhibitor–based combination therapy in lung cancer in a longitudinal clinical cohort. The absence of a comparable PRL trajectory in the colorectal cancer subgroup further highlights tumor-specific differences in immune–endocrine interactions. Despite preliminary mechanistic interpretation, these findings suggest that PRL may serve as a dynamic indicator of sustained systemic immune activation rather than overt endocrine dysfunction, underscoring the value of longitudinal hormone monitoring beyond early treatment time points.

Conversely, the lack of significant hormonal changes observed in the colorectal cancer subgroup suggests that endocrine responses to immunochemotherapy are not uniform across malignancies. Such heterogeneity highlights the importance of tumor context in interpreting endocrine alterations during systemic cancer treatment. Considering the relatively small sample size and exploratory design of the present study, these cancer-specific differences should be interpreted with caution and regarded as hypothesis-generating, warranting validation in larger prospective studies.

Sex-stratified analyses revealed distinct endocrine response patterns during PD-1 inhibitor–based immunochemotherapy. Male patients exhibited clearer longitudinal changes in pituitary hormones than female patients, with progressive increases observed over the course of treatment. In contrast, among female patients—who were postmenopausal—only limited changes were detected, with most hormonal parameters remaining relatively stable across follow-up. These findings indicate that early endocrine responses to combined chemotherapy and PD-1 blockade may differ according to biological sex and baseline endocrine status. Postmenopausal women exhibit physiological elevations in pituitary gonadotropins and reduced dynamic variability^[16], which may attenuate the magnitude of detectable treatment-related changes over short observation periods. In contrast, men, with lower baseline gonadotropin levels and intact feedback regulation, may demonstrate more readily apparent treatment-associated shifts in hypothalamic–pituitary activity. Taken together, the observed sex-related differences align with established physiological variation in hypothalamic–pituitary regulation rather than with sex-

specific endocrine toxicity. However, given the limited sample size, these findings should be interpreted with caution and warrant validation in larger cohorts.

In the present study, an additional observation of potential clinical relevance concerns the absence of significant declines in circulating sex steroids despite progressive changes in pituitary gonadotropins during PD-1 inhibitor–based immunochemotherapy. This pattern is different from the classical endocrine effects reported with cytotoxic chemotherapy alone, in which gonadal steroid suppression is frequently observed. Accordingly, it can be hypothesized that the addition of PD-1 blockade may not exacerbate—and may even attenuate—early chemotherapy-associated impairment of gonadal steroid production. One possible explanation is that immune checkpoint inhibition modulates systemic inflammatory and neuroendocrine stress responses^[17], thereby preserving peripheral steroidogenic function despite increased central gonadotropin signaling. Nevertheless, this interpretation remains exploratory. Determining whether PD-1–based regimens truly confer a protective or neutral effect on the HPG axis will require prospective studies with extended observation periods and comprehensive endocrine assessment.

In summary, our study reveals an association between PD-1 inhibitor–based immunochemotherapy and the selective modulation of circulating sex hormones that predominantly affects pituitary gonadotropins rather than causing widespread alterations in downstream sex steroids. Emerging during treatment, these endocrine changes exhibited heterogeneity according to cancer type and biological sex. Despite being modest in magnitude, the observed hormonal shifts highlight the sensitivity of the HPG axis to combined immune and cytotoxic therapies. Collectively, these findings underscore the importance of monitoring endocrine dynamics during immunochemotherapy, thereby providing a basis for future studies to clarify their longitudinal evolution and potential clinical relevance.

Declarations

Ethical Approval Statement

Ethical approval for this retrospective study was obtained from the Ethics Committee of the First Affiliated Hospital of Guangzhou University of Chinese Medicine (No. K-2026-104). The requirement for written informed consent to participate was waived by the Ethics Committee of the First Affiliated Hospital of Guangzhou University of Chinese Medicine because of the retrospective nature of the study and the use of anonymized clinical data. All procedures involving human participants were performed in accordance with the Declaration of Helsinki and relevant guidelines and regulations.

Data availability

The datasets used and/or analysed during the current study are not publicly available due to patient privacy and institutional data protection requirements. De-identified data may be available from the corresponding author upon reasonable request and with permission from the Ethics Committee of the First Affiliated Hospital of Guangzhou University of Chinese Medicine.

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Author Contribution

Deyu Yang conceived and designed the study. Deyu Yang and Xinrong Chen collected and organized the clinical data. Ke Wang and Chuangjie Zheng contributed to data verification and statistical analysis. Deyu Yang drafted the manuscript. Deyu Yang, Xinrong Chen, Zhichao Li, Mei Ouyang, Ke Wang and Chuangjie Zheng contributed to manuscript revision and interpretation of the results. Linzhu Zhai supervised the study, provided critical revisions, and approved the final version of the manuscript. All authors read and approved the final manuscript.

References

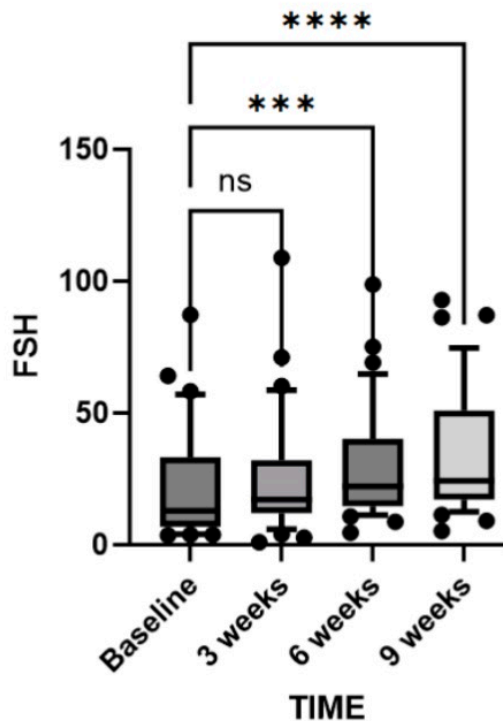
1. BRAY F, LAVERSANNE M. Global cancer statistics 2022: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries [J]. *CA Cancer J Clin*. 2024;74(3):229–63.
2. PABANI A, BUTTS C A. Current landscape of immunotherapy for the treatment of metastatic non-small-cell lung cancer [J]. *Curr Oncol*. 2018;25(Suppl 1):S94–102.
3. RAHIMI KALATEH SHAH MOHAMMAD G, GHAREMANLOO A, SOLTANI A, et al. Cytokines as potential combination agents with PD-1/PD-L1 blockade for cancer treatment [J]. *J Cell Physiol*. 2020;235(7–8):5449–60.
4. MÜLLER J. Impact of cancer therapy on the reproductive axis [J]. *Horm Res*. 2003;59(Suppl 1):12–20.
5. SCHILSKY R L, LEWIS B J, SHERINS RJ, et al. Gonadal dysfunction in patients receiving chemotherapy for cancer [J]. *Ann Intern Med*. 1980;93(1):109–14.

6. GAILLARD RC. [Interactions between the immune and neuroendocrine systems: clinical implications] [J]. J Soc Biol. 2003;197(2):89–95.
7. BEAGLEY K W, GOCKEL C M. Regulation of innate and adaptive immunity by the female sex hormones oestradiol and progesterone [J]. FEMS Immunol Med Microbiol. 2003;38(1):13–22.
8. CONFORTI F, PALA L. Cancer immunotherapy efficacy and patients' sex: a systematic review and meta-analysis [J]. Lancet Oncol. 2018;19(6):737–46.
9. SADIQ NM, Physiology TADIP. Pituitary Hormones [M]. StatPearls. Treasure Island (FL); StatPearls Publishing Copyright © 2026. StatPearls Publishing LLC; 2026.
10. RECALDE G, MORENO-SOSA T, YÚDICA F, et al. Contribution of sex steroids and prolactin to the modulation of T and B cells during autoimmunity [J]. Autoimmun Rev. 2018;17(5):504–12.
11. ODUWOLE O O PELTOKETO. HUHTANIEMI I T. Role of Follicle-Stimulating Hormone in Spermatogenesis [J]. Front Endocrinol (Lausanne). 2018;9:763.
12. PITTELOUD N, DWYER A A, DECRUZ S, et al. The relative role of gonadal sex steroids and gonadotropin-releasing hormone pulse frequency in the regulation of follicle-stimulating hormone secretion in men [J]. J Clin Endocrinol Metab. 2008;93(7):2686–92.
13. HUDDART RA, NORMAN A, MOYNIHAN C, et al. Fertility, gonadal and sexual function in survivors of testicular cancer [J]. Br J Cancer. 2005;93(2):200–7.
14. SCARBOROUGH D E. Cytokine modulation of pituitary hormone secretion [J]. Ann N Y Acad Sci. 1990;594:169–87.
15. PASCHOU SA, STEFANAKI K, PSALTOPOULOU T, et al. How we treat endocrine complications of immune checkpoint inhibitors [J]. ESMO Open. 2021;6(1):100011.
16. HALL JE. Endocrinology of the Menopause [J]. Endocrinol Metab Clin North Am. 2015;44(3):485–96.
17. BARNABEI A, CORSELLO A, PARAGLIOLA R M et al. Immune Checkpoint Inhibitors as a Threat to the Hypothalamus-Pituitary Axis: A Completed Puzzle [J]. Cancers (Basel), 2022, 14(4).

Figures

Figure 1

A



B

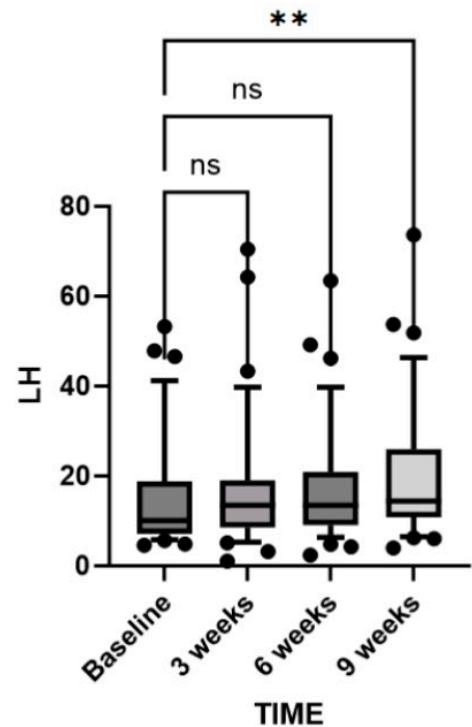


Figure 1

Longitudinal changes in pituitary-derived hormones in the overall cohort during PD-1 inhibitor-based immunochemotherapy.

(A) Levels of follicle-stimulating hormone (FSH) and (B) luteinizing hormone (LH) were measured at baseline (week 0) and at 3, 6, and 9 weeks after treatment initiation. Data are presented as box-and-whisker plots with individual data points. Statistical comparisons were performed using the Friedman test, followed by Dunn's multiple-comparisons test. ** $P < 0.01$, *** $P < 0.001$, **** $P < 0.0001$; ns, not significant.

Figure 2

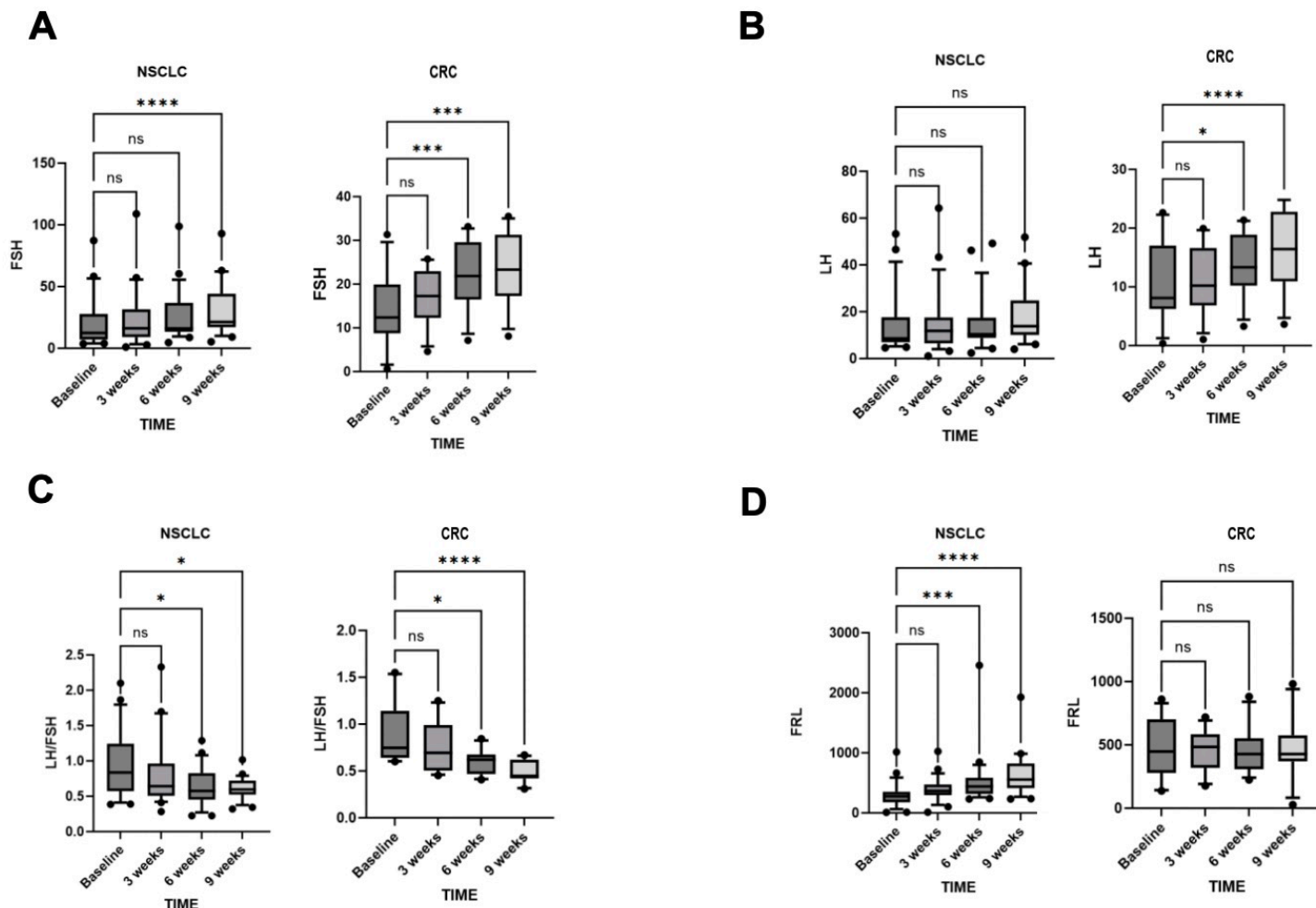
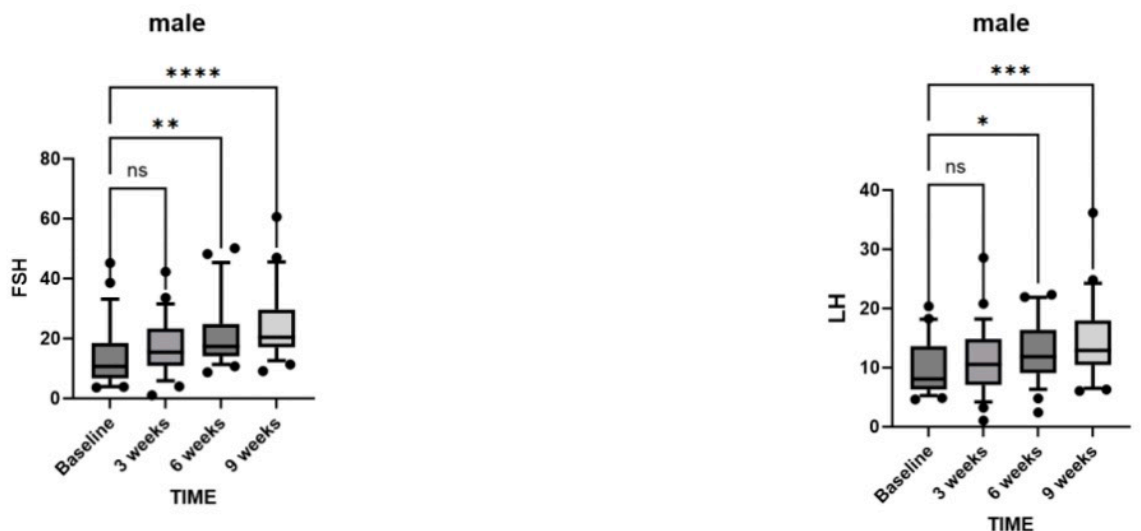


Figure 2

Longitudinal changes in pituitary-derived hormone levels in patients with non-small cell lung cancer (NSCLC) and colorectal cancer (CRC) during PD-1 inhibitor-based immunochemotherapy. (A–D) Serum levels of FSH, LH, the LH/FSH ratio, and PRL were measured at baseline (week 0) and at 3, 6, and 9 weeks after treatment initiation in patients with NSCLC and CRC. Data are presented as box-and-whisker plots with individual data points. Statistical comparisons were performed using the Friedman test, followed by Dunn's multiple-comparisons test. * $P < 0.05$, *** $P < 0.001$, **** $P < 0.0001$; ns, not significant.

Figure 3

A



B

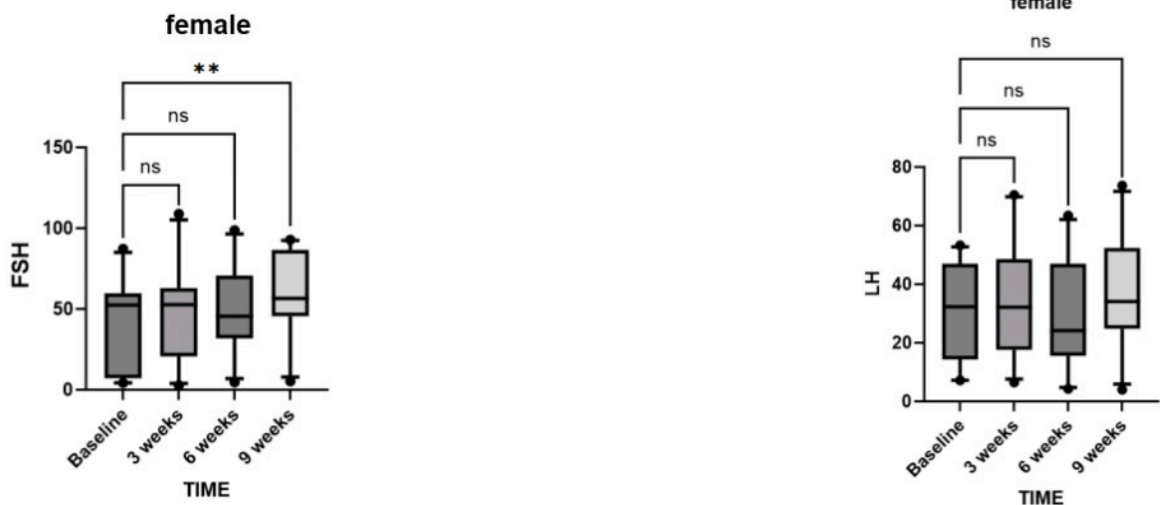


Figure 3

Sex-specific longitudinal changes in pituitary-derived hormone levels during PD-1 inhibitor–based immunochemotherapy.

(A) FSH and LH levels in male patients and (B) FSH and LH levels in female patients were measured at baseline (week 0) and at 3, 6, and 9 weeks after treatment initiation. Data are presented as box-and-whisker plots with individual data points. Statistical comparisons were performed using the Friedman test, followed by Dunn’s multiple-comparisons test. * $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$, **** $P < 0.0001$; ns, not significant.