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Research Article

Innovative Cancer Drugs: Medicolegal Assessments on Efficacy and Necessity

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Abstract

Objective: In recent years, targeted therapies and immune checkpoint inhibitors have provided significant gains in survival and quality of life compared to conventional chemotherapies. However, due to biomarker-based selectivity, high cost, and reimbursement restrictions, the concepts of "necessity" and "indication appropriateness" have become controversial from a medicolegal perspective. This study aimed to evaluate the clinical and forensic aspects of innovative cancer drug use by reviewing court case files.

Methods: A total of 455 case files submitted between January 1, 2022 and May 31, 2025, were retrospectively analyzed. Demographic data, cancer type and stage, histological subtype, performance status, previous treatments, innovative drug active agents, licensing and indication status, therapeutic intent, and council and board decisions were recorded. Data were evaluated using descriptive statistics.

Results: Of the cases, 53.6% were female and 46.4% male; the most common age group was ≥65 years. The most frequent malignancies were lung (35.2%) and breast (20.0%) cancers, and 69.5% of the patients were in stage IV disease. The most frequently used drugs were pembrolizumab (29.7%), nivolumab (16.0%), and atezolizumab (12.5%). Of all uses, 99.1% were licensed and 85.1% were indication-appropriate. Treatment intent was adjuvant in 48.6%, neoadjuvant in 10.1%, and post-progression in 41.1% of the cases. Multidisciplinary council decisions were documented in 47.3% of files, and the Forensic Board concluded that treatment use was "appropriate" in 97.6% of cases.

Conclusions: The findings indicate that innovative cancer drugs in Türkiye are mostly used within licensed and guideline-concordant indications. However, the lack of biomarker data and multidisciplinary council documentation constitutes an important limitation in medicolegal evaluations. Addressing these deficiencies would make therapeutic decisions more defensible both clinically and legally.

Keywords: Innovative cancer drugs, Smart drugs, Cancer, Indication appropriateness, Medicolegal evaluation

1. INTRODUCTION

In recent years, innovative cancer therapies—commonly referred to as "targeted" or "smart" drugs—including tyrosine kinase inhibitors, PARP inhibitors, CDK4/6 inhibitors, HER2-directed agents, and immune checkpoint inhibitors, have provided substantial improvements in survival and quality of life compared with conventional chemotherapy. The efficacy of these agents has been demonstrated through numerous randomized clinical trials, particularly in metastatic non-small cell lung cancer (NSCLC),[1,2] hepatocellular carcinoma (HCC),[3] breast cancer,[4] and ovarian cancer.[5]

However, due to their high cost, adverse effect profiles, and the need for biomarker-based patient selection, the necessity and appropriateness of these treatments remain subjects of clinical and ethical debate. In Türkiye, there has been a growing number of legal cases in recent years concerning these drugs, especially those that are not reimbursed or only partially covered by the Social Security Institution (SSI). In such lawsuits, filed by patients or their relatives seeking access to these medications, the scientific justification of the treatment decision, the drug's licensing status, and its compliance with national and international guidelines are frequently evaluated by expert witnesses.

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The 7th Specialization Board of the Council of Forensic Medicine reviews oncological data, treatment indications, genetic and histopathological findings, and the scientific validity of the prescribed drugs to provide expert opinions for the courts. This study retrospectively examines case files submitted to the 7th Specialization Board between 2022 and 2025, aiming to evaluate the effectiveness and necessity of innovative cancer therapies from a forensic medical perspective. In doing so, it seeks to contribute to clinical decision-making processes and to strengthen medico-legal defensibility in such cases.

2. MATERIALS AND METHODS

2.1. Study design

This research is a retrospective and descriptive study. Among 27,500 legal case files submitted to the 7th Specialization Board between January 1, 2022 and May 31, 2025, a total of 455 cases in which expert evaluation was requested regarding the use of innovative cancer drugs were examined. For each case, medico-legal records, oncology discharge summaries, pathology reports, treatment records, and multidisciplinary council decisions were obtained from the files forwarded by the courts. The final expert opinions and board decisions were retrieved from the evaluation reports of the 7th Specialization Board.

2.2. Variables analyzed

- Demographic data: Age and sex
- Medical data: Cancer type and stage, histological subtype, performance status (ECOG/Karnofsky), comorbidities, previous treatments (surgery, chemotherapy, radiotherapy, hormone therapy), and disease course (progression, recurrence, remission)
- Innovative cancer drug data: Active substance used, licensing status (approved or unapproved in Türkiye), indication appropriateness (based on international guidelines), and therapeutic purpose (neoadjuvant, adjuvant, post-progression, or palliative use)
- Decision-making processes: Multidisciplinary council decision and 7th Specialization Board decision

The appropriateness of indication was assessed according to the conformity between the clinical use reported in each file and the corresponding ESMO and NCCN guidelines, as well as national licensing conditions valid in the treatment year.

2.3. Statistical analysis

Data were analyzed using SPSS (version [26.0]). Descriptive statistics were presented as numbers and percentages. Categorical variables were compared using Pearson's chi-square or Fisher's exact test, as appropriate. A p-value of <0.05 was considered statistically significant.

2.4. Ethical approval

This study was reviewed and approved by the Committee of Education and Scientific Research, Council of Forensic Medicine on August 12, 2025 (approval number: 21589509/2025/947). All patient identifiers were removed, and the data were anonymized prior to analysis.

3. RESULTS

Among the 455 cases included in the study, 244 were female (53.6%) and 211 were male (46.4%). Regarding age distribution, the largest groups were patients aged ≥65 years (30.8%) and those aged 56–65 years (28.8%). Younger age groups each accounted for less than 10% of the total (Table 1).

Table 1.

Distribution of demographic variables

Variable		n	%
Sex	Female	244	53.6
	Male	211	46.4
Age group	0-18	20	4.4
	19-25	22	4.8
	26-35	30	6.6
	36-45	40	8.8
	46-55	72	15.8
	56-65	131	28.8
	65 +	140	30.8

The most common malignancy was lung cancer, representing 160 cases (35.2%), followed by breast cancer in 91 cases (20.0%). Less frequent cancers included ovarian (n = 19, 4.2%), liver (n = 18, 4.0%), skin (n = 17, 3.7%), and renal cancers (n = 15, 3.3%). Additional diagnoses were pleural malignant mesothelioma (n = 13, 2.9%), gastric cancer (n = 12, 2.6%), colon and bladder cancers (each n = 11, 2.4%), cervical cancer (n = 10, 2.2%), and Hodgkin lymphoma (n = 9, 2.0%). Endometrial (n = 8), laryngeal (n = 7), nasopharyngeal (n = 7), and malignant melanoma (n = 6) cases were less frequent. Rare malignancies included lymphomas, thyroid carcinoma, malignant peritoneal mesothelioma, and multiple myeloma. Early-stage cases (below stage II) were uncommon (<5%). Among lung cancer cases, the predominant histological subtypes were adenocarcinoma and squamous cell carcinoma; small-cell carcinoma and neuroendocrine variants were less frequent. In breast cancer, invasive ductal and invasive carcinoma of no special type were most common, with some triple-negative tumors recorded. High-grade serous carcinoma was the dominant subtype among ovarian cancers, while nearly all liver cases were hepatocellular carcinoma. Mesothelioma cases were mostly of the epithelioid type. Malignant melanomas were categorized under the general "malignant melanoma" heading, and hematologic malignancies (Hodgkin/non-Hodgkin lymphomas, multiple myeloma) were recorded without further subtyping (Table 2).

Table 2.

Distribution of cancer types and histological subtypes

Cancer Type	**Histological Subtype**	**n**	**%**
Lung cancer (n = 160, 35.2%)	Adenocarcinoma	80	50
	Squamous cell carcinoma	48	30
	Small-cell carcinoma	24	15
	Other	8	5
Breast cancer (n = 91, 20.0%)	Invasive ductal carcinoma	64	70.5
	Invasive lobular carcinoma	18	19.7
	Other	9	9.8
Ovarian cancer (n = 19, 4.2%)	High-grade serous carcinoma	19	100
Liver cancer (n = 18, 4.0%)	Hepatocellular carcinoma	18	100
Skin cancer (n = 17, 3.7%)	Subtype not specified	17	100
Renal cancer (n = 15, 3.3%)	Subtype not specified	15	100
Mesothelioma (n = 13, 2.9%)	Epithelioid type	10	77
	Sarcomatoid / mixed type	3	23
Others* (n = 122, 26.8%)	Subtype not specified	122	100

*"Others" include gastric, colorectal, bladder, cervical, lymphoid, endometrial, laryngeal, and malignant melanoma cases.

Most patients were in advanced stages: stage IV in 316 cases (69.5%) and stage III in 40 cases (8.8%). Performance status data (ECOG) were available for 430 cases: 86.3% were ECOG 0, 12.1% ECOG 1, and 1.6% ECOG 2; no cases with ECOG ≥ 3 were observed. ECOG data were missing in 25 cases. Regarding disease course, progression was seen in 204 cases (44.8%), remission in 175 (38.5%), and recurrence in 17 (3.7%).

Analysis of previous treatments showed that single-modality therapy was applied in 136 cases (29.9%), mostly chemotherapy (CT) alone; a few had surgery or radiotherapy (RT) only. Dual-modality therapy was the most frequent pattern (n = 188, 41.3%), mainly surgery + CT or CT + RT,

and less commonly surgery + RT or CT + hormone therapy (HT). Triple-modality treatment (surgery + CT + RT) was recorded in 85 cases (18.7%), while quadruple treatment (surgery + CT + RT + HT) was rare (n = 27, 5.9%). Cases with no documented prior therapy represented 4.2% (n = 19) (Table 3).

Table 3.

Distribution of treatment modalities

Treatment Modality	n	%
Single-modality therapy (CT / RT / HT / Surgery)	136	29.9
Dual-modality therapy (Surgery + CT / CT + RT / Surgery + RT / CT + HT)	188	41.3
Triple-modality therapy (Surgery + CT + RT)	85	18.7
Quadruple-modality therapy (Surgery + CT + RT + HT)	27	5.9
Unknown / not documented	19	4.2

Pembrolizumab was the most frequently used innovative drug, administered in 135 cases (29.7%). It was followed by nivolumab in 73 cases (16.0%) and atezolizumab in 57 cases (12.5%). Less common agents included olaparib (n = 19, 4.2%), durvalumab (n = 18, 4.0%), and the combination nivolumab + ipilimumab (n = 16, 3.5%). Abemaciclib, osimertinib, and pembrolizumab + pemetrexed combinations were each used in 10 cases (2.2%). Rarely used agents were niraparib (n = 7, 1.5%), alpelisib (n = 6, 1.3%), and atezolizumab + bevacizumab (n = 6, 1.3%). Other agents such as pemetrexed, ruxolitinib, ribociclib, trastuzumab emtansine, and pertuzumab were observed in 5 cases each (1.1%). Additional drugs included abemaciclib, deruxtecan, and lenvatinib (each n = 4, 0.9%), as well as avelumab, sacituzumab govitecan, and cabozantinib (each n = 3, 0.7%). Palbociclib, ramucirumab, and the nivolumab + cabozantinib combination were used in two cases each (0.4%), while several others appeared only once (0.2%) (Table 4).

Table 4.

Distribution of innovative drug use

Drug / Active Agent	n	%
Pembrolizumab	135	29.7
Nivolumab	73	16.0
Atezolizumab	57	12.5
Olaparib	19	4.2
Durvalumab	18	4.0
Nivolumab+Ipilimumab	16	3.5
Abemaciclib	10	2.2
Osimertinib	10	2.2
Pembrolizumab+Pemetrexed	10	2.2
Others*	80	17.6

*"Others" include niraparib, alpelisib, bevacizumab, pemetrexed, ruxolitinib, ribociclib, trastuzumab, pertuzumab, lenvatinib, avelumab, sacituzumab govitecan, cabozantinib, ramucirumab, and cabozantinib combinations.

Among all agents, 99.1% (n = 452) were licensed in Türkiye, whereas unlicensed use was identified in 1.9% (n = 9). The therapeutic intent was adjuvant in 221 cases (48.6%), neoadjuvant in 46 (10.1%), and post-progression in 187 (41.1%). Treatment indications were consistent with international guidelines in 387 cases (85.1%) and inconsistent in 68 (14.9%).

A multidisciplinary council decision was present in 215 cases (47.3%) and absent in 239 (52.5%) (Table 5). According to the evaluations of the xxx Forensic Board, drug use was considered

"appropriate" in 444 cases (97.6%), "not assessable" in 10 cases (2.2%), and "inappropriate" in only one case (0.2%) (Table 5).

Table 5.

Distribution of cases by decision type

Type of Decision		n	%
Multidisciplinary council decision	Present	215	47.3
	Absent	239	52.5
Forensic board decision	Appropriate	444	97.6
	Inappropriate	1	0.2
	Not assessable	10	2.2

4. DISCUSSION

This study provides comprehensive data on the effectiveness and necessity of innovative cancer therapies through a retrospective analysis of 455 legal case files. The findings extend beyond drug types and cancer diagnoses, encompassing variables such as demographics, performance status, prior treatments, treatment purpose, and both council and forensic board decisions—factors that directly influence clinical practice and medico-legal evaluations.

More than half of the patients were female (53.6%), which can be attributed to the high proportion of breast cancer cases, the second most frequent cancer type in this series. In general, breast and gynecologic malignancies predominate among females, whereas lung and liver cancers are more common in males.[6] The most frequent age groups were ≥65 years (30.8%) and 56–65 years (28.8%), consistent with epidemiological data showing that cancer incidence increases markedly with age.[7] This older patient profile also strengthens the "necessity" debate in medico-legal evaluations of immunotherapy and targeted agents, as comorbidities in the elderly may significantly affect both drug efficacy and toxicity.

Lung cancer was the most frequent malignancy (35.2%), followed by breast cancer (20.0%), a distribution consistent with both global[7] and national[8] epidemiological data. Ovarian (4.2%), liver (4.0%), skin (3.7%), and renal (3.3%) cancers were less common, in line with the generally lower incidence of gynecologic and hepatobiliary tumors in Türkiye.[9] The frequency of pleural mesothelioma (2.9%) is notable, reflecting the higher incidence of this cancer in regions of Türkiye—particularly Southeastern and Central Anatolia—where environmental asbestos exposure remains an established risk factor.[10]

Most patients were at an advanced stage, with stage IV disease accounting for 69.5%. This finding suggests that medico-legal cases often involve patients diagnosed or treated at advanced stages, where treatment decisions are more likely to be contested. In developing countries, late-stage diagnoses in lung and breast cancers are more frequent, often linked to delays in presentation, inadequate screening, and limited access to therapy.[6]

Histopathological distributions were compatible with international data: adenocarcinoma and squamous cell carcinoma were the predominant subtypes in lung cancer.[11] In breast cancer, invasive ductal carcinoma was the most frequent histological type, and the presence of triple-negative tumors was noteworthy; given their biological aggressiveness and limited treatment options, these cases often justify the use of innovative therapies.[12] High-grade serous carcinoma was the predominant subtype in ovarian cancer, as reported in global and Turkish series.[13] Nearly all liver tumors were hepatocellular carcinoma, confirming its known histologic dominance.[14] Most mesothelioma cases were of the epithelioid type, which is associated with a relatively better prognosis.[10] Rarer entities such as malignant melanoma and hematologic malignancies were less represented. However, the lack of specific subtype data for hematologic cases limited the detailed assessment of indication appropriateness and therapeutic necessity.

Performance status data showed that 86.3% of patients were ECOG 0 and 12.1% were ECOG 1, with virtually no cases ≥ ECOG 2. This indicates that most patients reviewed were in good clinical condition. Clinical trials have demonstrated that immunotherapies and targeted agents are primarily effective in ECOG 0–1 populations.[2,15]

Accordingly, the predominance of well-performing patients supports the justification for treatment in these cases. Nevertheless, in real-world settings, patients with ECOG ≥2 may also require treatment, and decisions for this group may remain more controversial in medico-legal contexts.

Dual-modality treatment was observed in 41.3% of cases, triple-modality in 18.7%, and quadruple-modality in 5.9%, while single-modality therapy accounted for 29.9%. This distribution reflects the increasing adoption of multimodal strategies in contemporary oncology practice. The high rates of surgery + chemotherapy and chemotherapy + radiotherapy combinations are consistent with international standards.[16] In our series, 41.1% of patients received immunotherapy or innovative drugs after disease progression, mirroring second-line benefits reported in pivotal trials such as KEYNOTE-045 (urothelial carcinoma)[17] and CheckMate-141 (head and neck cancers).[18]

Innovative drugs in this cohort were administered with adjuvant intent in 48.6%, neoadjuvant in 10.1%, and post-progression in 41.1% of cases. This pattern aligns with the expanding evidence base supporting immunotherapy in early-stage adjuvant and neoadjuvant settings.[19] For instance, the IMpower010 trial demonstrated a disease-free survival benefit with adjuvant atezolizumab in resected NSCLC,[20] while the OlympiA trial showed an overall survival advantage with adjuvant olaparib in BRCA-mutated early breast cancer.[21] Thus, the relatively high proportion of adjuvant use in our data parallels global trends and reinforces the "necessity" argument for such therapies.

Among lung cancer cases, pembrolizumab (n = 126), nivolumab (n = 69), and atezolizumab (n = 52) were the most commonly used agents. This reflects current treatment algorithms, where immune checkpoint inhibitors have become the standard first-line therapy for advanced NSCLC. The KEYNOTE-024 trial demonstrated superior overall survival (OS) for pembrolizumab over chemotherapy in PD-L1 ≥50% NSCLC,[1] while KEYNOTE-189 confirmed an OS benefit regardless of PD-L1 status when pembrolizumab was combined with chemotherapy.[22] Similarly, CheckMate-227 reported long-term OS improvement with the nivolumab + ipilimumab combination in selected subgroups.[23] The predominance of advanced-stage lung cancers in our series likely explains the high rate of immunotherapy use. However, the absence of biomarker data prevented assessment of whether treatment decisions aligned with PD-L1 expression or tumor mutational burden (TMB).

Breast cancer, the second most frequent malignancy (n = 91, 20.0%), included cases treated with abemaciclib (n = 10), trastuzumab emtansine (T-DM1), and other novel anti-HER2 agents. Current evidence shows that adjuvant abemaciclib significantly prolongs invasive disease-free survival (IDFS) in high-risk, HR-positive, HER2-negative early-stage breast cancer.[24] The KATHERINE trial demonstrated that adjuvant T-DM1 significantly improved IDFS compared with trastuzumab in patients with residual disease after neoadjuvant therapy.[4] In metastatic HER2-positive disease, the DESTINY-Breast03 trial showed that trastuzumab deruxtecan (T-DXd) achieved superior OS and PFS compared with T-DM1.[25] Given that most of our cases involved advanced stages, the predominant use of these agents in metastatic settings is consistent with current evidence. However, the lack of biomarker data limited evaluation of how HER2 status influenced treatment selection.

In ovarian cancer (n = 19, 4.1%), olaparib (n = 18) and niraparib (n = 7) were the most commonly used agents. Clinical data show that PARP inhibitors offer significant survival benefits in patients with BRCA mutations or homologous recombination deficiency (HRD).

The seven-year follow-up of the SOLO1 trial confirmed durable PFS and OS benefits with olaparib maintenance in BRCA-mutated advanced ovarian cancer.[5] The OlympiA trial also reported OS improvement with adjuvant olaparib in early-stage BRCA-mutated breast cancer.[21] In contrast, the PRIMA trial demonstrated a PFS benefit but no OS advantage for niraparib.[26] Therefore, evaluation of PARP inhibitor "necessity" must consider patient subgroups, molecular profiles, and toxicity risks. In our dataset, the absence of

biomarker information restricted assessment of indication appropriateness for these agents.

In hepatocellular carcinoma (HCC) (n = 18, 4.0%), the atezolizumab + bevacizumab combination (n = 6) was the most frequent regimen. The IMbrave150 study showed that this combination improved both OS and PFS compared with sorafenib,[3] with a 36-month OS rate of 28.5%.[27] Although relatively few cases in our series received this regimen, the strong evidence base and the limitations of reimbursement policies in Türkiye suggest that such treatments represent clinically justified use from a medico-legal perspective.

Almost all drugs used were licensed in Türkiye (99.1%), and off-label use was detected in only 1.9% of cases. The rate of guideline-concordant use was 85.1%, consistent with literature reports that off-label prescribing in oncology—though variably defined—remains substantial. Levêque[28] highlighted that rational, genotype-driven off-label use is increasing, yet challenges persist regarding evidence strength, reimbursement, and ethical considerations.

Notably, in 52.5% of cases, no multidisciplinary tumor board documentation was available. This represents a critical deficiency in terms of treatment traceability and medico-legal defensibility. Previous studies have demonstrated that tumor boards improve standardization of treatment decisions and enhance survival outcomes.[29] In contrast, the 7th Specialization Board considered drug use "appropriate" in 97.6% of cases, "not assessable" in 2.2%, and "inappropriate" in only 0.2%. This high rate of appropriateness suggests that treatment decisions were generally guideline-based and scientifically grounded. Nonetheless, the absence of council documentation remains a serious limitation, particularly in the context of forensic and legal scrutiny.

5. CONCLUSION

Our findings are consistent with the efficacy evidence reported in recent clinical trials and support the concept of "necessity" from a forensic medical perspective. However, the lack of biomarker data limited the ability to assess how treatment choices corresponded to predictive parameters such as PD-L1, BRCA, HRD, or HER2 status. In addition, the absence of documented multidisciplinary council decisions in 52.5% of cases emerged as a major deficiency, making it more difficult for physicians to defend their decisions in medico-legal proceedings.

From a forensic medicine standpoint, the significance of this study lies in systematically presenting key parameters—such as therapeutic necessity, drug licensing, and indication concordance—in the context of innovative cancer therapies, supported by scientific evidence.

The absence of council documentation and insufficient biomarker reporting highlight recurring gaps frequently debated in expert evaluations. These results indicate that improving documentation and data recording systems is essential to ensure that expert opinions submitted to the courts are grounded on a transparent and scientifically robust foundation. Such improvements would ultimately contribute to a fairer, more traceable, and defensible framework, safeguarding both patients' right to access treatment and physicians' medico-legal accountability.

Article Information Form

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Author Contributions

Conceptualization: C.B., H.A.; Data curation: M.B.C., M.E.; Investigation: M.B.C., M.E.B., M.E., E.G.; Formal analysis: C.B., M.E., Writing- original draft: C.B., M.E.B., M.B.C; Writing- review and editing: M.G., E.G., H.A.; Supervision: M.G., E.G., H.A.

The Declaration of Conflict of Interest/ Common Interest

No conflict of interest or common interest has been declared by authors.

The Declaration of Ethics Committee Approval

This study was reviewed and approved by the Committee of Education and Scientific Research, Council of Forensic Medicine on August 12, 2025 (approval number: 21589509/2025/947).

Artificial Intelligence Statement

No artificial intelligence tools were used while writing this article.

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REFERENCES

1. Reck M, Rodriguez- Abreu D, Robinson AG, Hui R, Csőszi T, Fülöp A, et al. Updated analysis of KEYNOTE-024: pembrolizumab versus platinum-based chemotherapy for advanced non-small-cell lung cancer with PD-L1 tumor proportion score of 50% or greater. J Clin Oncol. 2019;37(7):537-46. doi:10.1200/JCO.18.00149.
2. Spigel DR, Faivre- Finn C, Gray JE, Vicente D, Planchard D, Paz-Ares L, et al. Five-year survival outcomes from the PACIFIC trial: durvalumab after chemoradiotherapy in stage III non-small-cell lung cancer. J Clin Oncol. 2022;40(12):1301-11. doi:10.1200/JCO.21.01308.
3. Finn RS, Qin S, Ikeda M, Galle PR, Ducreux M, Kim TY, et al. Atezolizumab plus bevacizumab in unresectable hepatocellular carcinoma. N Engl J Med. 2020;382(20):1894-905. doi:10.1056/NEJMoa1915745.
4. von Minckwitz G, Huang CS, Mano MS, Loibl S, Mamounas EP, Untch M, et al. Trastuzumab emtansine for residual invasive HER2-positive breast cancer. N Engl J Med. 2019;380(7):617-28. doi:10.1056/NEJMoa1814017.
5. DiSilvestro P, Banerjee S, Colombo N, Scambia G, Kim BG, Oaknin A, et al. Overall survival with maintenance olaparib at a 7-year follow-up in patients with newly diagnosed advanced ovarian cancer and a BRCA mutation: the SOLO1/GOG 3004 trial. J Clin Oncol. 2023;41(3):609-17. doi:10.1200/JCO.22.01549.
6. Bray F, Laversanne M, Sung H, Ferlay J, Siegel RL, Soerjomataram I, et al. Global cancer statistics 2022: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin. 2024;74(3):229-63. doi:10.3322/caac.21834.
7. Siegel RL, Kratzer TB, Giaquinto AN, Sung H, Jemal A. Cancer statistics, 2025. CA Cancer J Clin. 2025;1-36. doi:10.3322/caac.21871.
8. T.C. Sağlık Bakanlığı Halk Sağlığı Genel Müdürlüğü, Kanser Daire Başkanlığı. Türkiye kanser istatistikleri 2020. Ankara: Halk Sağlığı Genel Müdürlüğü; 2025.
9. Eser S, Örün H, Hamavioğlu E, Lotfi F. Cancer incidence, mortality and survival in Türkiye as of 2020. BCCR. 2022;1(14):1-13. doi:10.18502/bccr.v14i1.14383.
10. Senyiğit A, Babayiğit C, Gökirmak M, Topçu F, Asan E, Coşkunsel M, et al. Incidence of malignant pleural mesothelioma due to environmental asbestos fiber exposure in the southeast of Turkey. 2000;67(6):610-4. doi:10.1159/000056289.
11. Travis WD, Brambilla E, Nicholson AG, Yatabe Y, Austin JHM, Beasley MB, et al. The 2015 World Health Organization classification of lung tumors: impact of genetic, clinical and radiologic advances since the 2004 classification. J Thorac Oncol. 2015;10(9):1243-60. doi:10.1097/JTO.0000000000000630.
12. Bianchini G, De Angelis C, Licchetta A, Gainni L. Treatment landscape of triple-negative breast cancer—expanded options, evolving needs. Nat Rev Clin Oncol. 2022;19(2):91-113. doi:10.1038/s41571-021-00565-2.
13. Matulonis UA, Sood AK, Fallowfield L, Howitt BE, Sehouli J, Karlan BY. Ovarian cancer. Nat Rev Dis Primers. 2016;2:16061. doi:10.1038/nrdp.2016.61.
14. Villanueva A. Hepatocellular carcinoma. N Engl J Med. 2019;380(15):1450-62. doi:10.1056/NEJMra1713263.
15. Brahmer J, Reckamp KL, Baas P, Crinò L, Eberhardt WE, Poddubskaya E, et al. Nivolumab versus docetaxel in advanced squamous-cell non-small-cell lung cancer. N Engl J Med. 2015;373(2):123-35. doi:10.1056/NEJMoa1504627.
16. Daly ME, Singh N, Ismaila N, Antonoff MB, Arenberg DA, Bradley J, et al. Management of stage III non-small-cell lung cancer: ASCO

guideline. J Clin Oncol. 2022;40(12):1356-84. doi:10.1200/JCO.21.02528.
17. Bellmunt J, de Wit R, Vaughn DJ, Fradet Y, Lee JL, Fong L, et al. Pembrolizumab as second-line therapy for advanced urothelial carcinoma. N Engl J Med. 2017;376(11):1015-26. doi:10.1056/NEJMoa1613683.
18. Ferris RL, Blumenschein G Jr, Fayette J, Guigay J, Colevas AD, Licitra L, et al. Nivolumab for recurrent squamous-cell carcinoma of the head and neck. N Engl J Med. 2016;375(19):1856-67. doi:10.1056/NEJMoa1602252.
19. Shukla N, Hanna N. Neoadjuvant and adjuvant immunotherapy in early-stage non-small cell lung cancer. Lung Cancer (Auckl). 2021;12:51–60. doi:10.2147/LCTT.S277717
20. Felip E, Altorki N, Zhou C, Csőszi T, Vynnychenko I, Goloborodko O, et al. Adjuvant atezolizumab after adjuvant chemotherapy in resected stage IB-IIIA non-small-cell lung cancer (IMpower010): a randomised, multicentre, open-label, phase 3 trial. Lancet. 2021;398(10308):1344-57. doi:10.1016/S0140-6736(21)02098-5.
21. Tutt ANJ, Garber JE, Kaufman B, Viale G, Fumagalli D, Rastogi P, et al. Adjuvant olaparib for patients with BRCA1- or BRCA2-mutated breast cancer. N Engl J Med. 2021;384(25):2394-405. doi:10.1056/NEJMoa2105215.
22. Gandhi L, Rodríguez-Abreu D, Gadgeel S, Esteban E, Felip E, De Angelis F, et al. Pembrolizumab plus chemotherapy in metastatic non-small-cell lung cancer. N Engl J Med. 2018;378(22):2078-92. doi:10.1056/NEJMoa1801005.
23. Hellmann MD, Paz-Ares L, Caro RB, Zurawski B, Kim SW, Carcereny Costa E, et al. Nivolumab plus ipilimumab in advanced non-small-cell lung cancer. N Engl J Med. 2019 Nov 21;381(21):2020-31. doi:10.1056/NEJMoa1910231.
24. Johnston SRD, Harbeck N, Hegg R, Toi M, Martin M, Shao ZM, et al. Abemaciclib combined with endocrine therapy for the adjuvant treatment of HR+, HER2-, node-positive, high-risk, early breast cancer (monarchE). J Clin Oncol. 2020;38(34):3987-98. doi:10.1200/JCO.20.02514.
25. Hurvitz SA, Kim SB, Chung WP, Im SA, Park YH, Hegg R, et al. Trastuzumab deruxtecan versus trastuzumab emtansine in HER2-positive metastatic breast cancer patients with brain metastases from the randomized DESTINY-Breast03 trial. ESMO Open. 2024;9(5):102924. doi:10.1016/j.esmoop.2024.102924.
26. González-Martín A, Pothuri B, Vergote I, DePont Christensen R, Graybill W, Mirza MR, et al. Niraparib in patients with newly diagnosed advanced ovarian cancer. N Engl J Med. 2019;381(25):2391-402. doi:10.1056/NEJMoa1910962.
27. Storand MH, Zemla TJ, Patell K, Naleid N, Gile JJ, Tran NH, et al. Atezolizumab plus bevacizumab as first-line systemic therapy for hepatocellular carcinoma: a multi-institutional cohort study. Oncologist. 2024;29(11):986-96. doi:10.1093/oncolo/oyae142.
28. Levêque D. Off-label use of targeted therapies in oncology. World J Clin Oncol. 2016;7(2):253-7. doi:10.5306/wjco.v7.i2.253.
29. Krause A, Stocker G, Gockel I, Seehofer D, Hoffmeister A, Bläker H, et al. Guideline adherence and implementation of tumor board therapy recommendations for patients with gastrointestinal cancer. J Cancer Res Clin Oncol. 2023;149(3):1231-40. doi:10.1007/s00432-022-03991-6.