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Cancer of Unknown Primary Most Suggestive of Colorectal Origin With Microsatellite Instability-high Status and High Tumor Mutation Burden Including NTRK Fusion

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Abstract

Background/Aim: Cancer of unknown primary (CUP) is associated with a poor prognosis. Recent advances in comprehensive genomic profiling (CGP) have made it possible to detect actionable mutations in CUP cases, which allows the inference of the primary tumor site. This report demonstrates CUP most suggestive of colorectal origin and highlights how CGP can significantly impact treatment decisions and outcomes.

Case Report: A 73-year-old woman presented with altered consciousness secondary to diabetic ketoacidosis. Imaging revealed a huge mass with abscess formation near the hepatic flexure, but colonoscopy and biopsy failed to identify a definitive primary site. The histopathology of echo-guided percutaneous tumor biopsy showed poorly differentiated adenocarcinoma. Immunohistochemistry revealed that it was positive for cytokeratin (CK) 7, negative for CK20, and slightly positive for caudal type homeobox (CDX) 2. Although colorectal cancer was the most suspected diagnosis based on imaging examination, the patient was still diagnosed with CUP and treated with carboplatin and nab-paclitaxel, resulting in a partial response; however, treatment was discontinued due to adverse effects. CGP revealed microsatellite instability (MSI)-high, high tumor mutation burden (TMB) of 100/Mb, and neurotrophic tropomyosin receptor tyrosine kinase (*NTRK*) fusion. The patient was subsequently treated with larotrectinib, to achieve further tumor shrinkage. Considering MSI-high and *TPM3-NTRK1* fusion in addition to radiological examinations, colorectal cancer was the most suspected diagnosis.

Conclusion: CUP is generally associated with poor prognosis. Comprehensive genomic profiling (CGP) offers a promising avenue for discovering personalized and potentially effective therapeutic strategies.

Keywords: CUP, CGP, TPM3-NTRK1, MSI-high, larotrectinib, colon cancer.

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Introduction

Cancer of unknown primary (CUP) refers to metastatic malignancies in which the primary tumor site cannot be identified, despite thorough clinical and radiological examination (1). CUP presents as a heterogeneous group of cancers and is generally considered to have a poor prognosis. A previous report showed that the 1-year survival rate of patients with CUP is less than 20% and that CUP is associated with a high risk of drug resistance, contributing to its unfavorable clinical outcomes (2).

The inability to identify the primary tumor limits the effectiveness of conventional treatment strategies, which often rely on a presumptive diagnosis of the site of origin. In recent years, comprehensive genomic profiling (CGP) using next-generation sequencing (NGS) has emerged as a promising tool for identifying specific genetic alterations in cancers with a poor prognosis, including CUP (2). This allows for the possibility of tailoring treatment based on the molecular characteristics of the tumor rather than its presumed site of origin. It has been shown that such personalized treatment approaches may offer better outcomes than conventional therapies (3). We herein present a case of CUP most suggestive of colorectal origin and in which CGP was crucial for the identification of actionable mutations, leading to a selection of treatment regimen.

Case Report

A 73-year-old woman with a history of diabetes presented to our hospital with impaired consciousness secondary to diabetic ketoacidosis. Computed tomography (CT) was performed to investigate the cause of her altered mental state, and a huge tumor with abscess formation was found near the transverse colon at the hepatic flexure (Figure 1). No other tumorous lesions were detected in the CT images, including those of the neck, chest, abdomen, and pelvic cavity. After treatment for diabetic ketoacidosis, total colonoscopy was performed, which revealed circumferential edema and stenosis near the hepatic flexure without a tumorous lesion in the colonic mucosa. Beyond the stenotic area, the abscess was connected, and the proximal intestine could not be confirmed. Esophagogastroduodenoscopy revealed no tumorous lesions in the esophagus or stomach. However, edema extending from the duodenal bulb to the descending duodenum was observed. A fistula was identified in the bulb that was suspected to be connected to the abscess. However, the tumor could not be accessed. Her carcinoembryonic antigen (CEA) level was within the normal limits (3.6 ng/ml), while her carbohydrate antigen 19-9 (CA 19-9) level was elevated at 91 U/ml. After some reduction in abscess size following conservative fasting and antibiotic therapy, repeat colonoscopy was performed. However, a definitive diagnosis could not be made through histological examination and imaging. The patient was scheduled to undergo surgery based on the expectation of oral intake and the histological diagnosis. However, surgery was delayed due to coronavirus (COVID)-19 infection, which resulted in prolonged treatment.

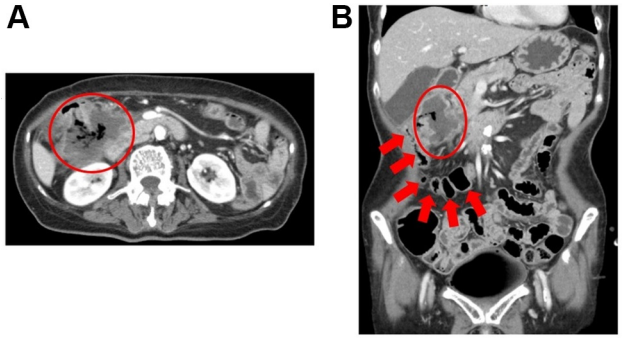

Figure 1. *Abdominal computed tomography showing a large tumor near the transverse colon at the hepatic flexure. Axial image (A), and coronal plane (B). The tumor is surrounded by red circles. Red arrows indicate the transverse colon.*

Approximately two months after the initial admission, laparoscopic gastrojejunostomy and ileostomy were performed because radical resection of the tumorous lesion and abscess formation were difficult due to the patient's general condition. During the operation, the tumor and abscess were identified as masses near the hepatic flexure. Echo-guided percutaneous tumor biopsy was performed, and a pathological examination revealed

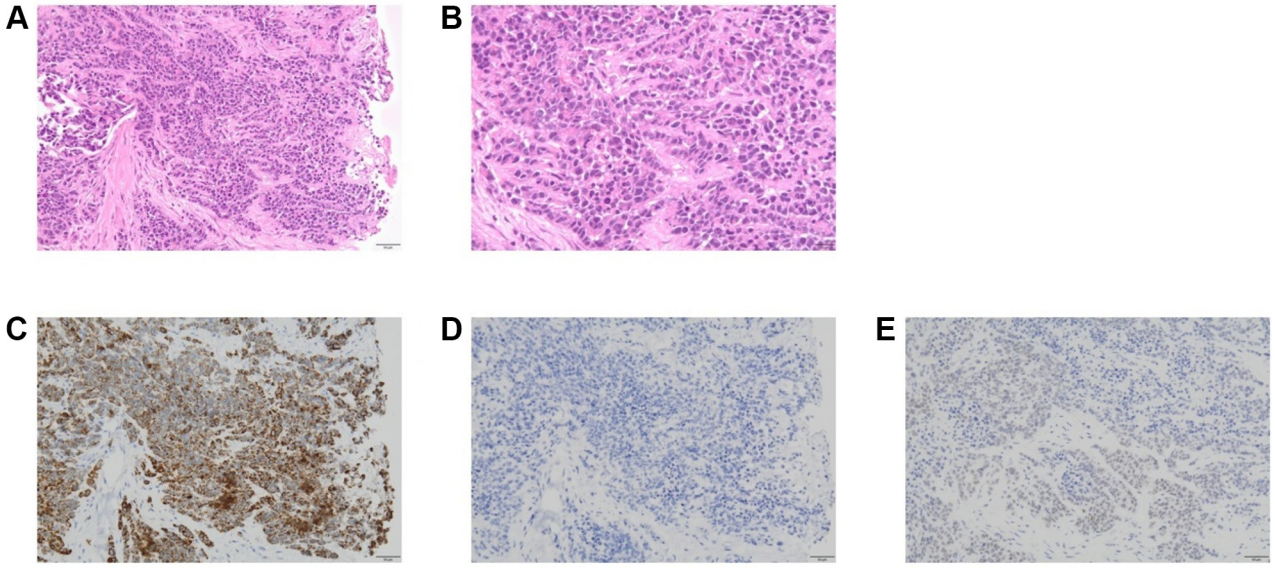

Figure 2. *Histological examination of the tumor biopsy specimen. Hematoxylin and eosin staining [200× magnification (A), 400× (B)]. The tissue was positive for CK7 (200×) (C), negative for CK20 (200×) (D), and partially positive for CDX2 (200×) (E).*

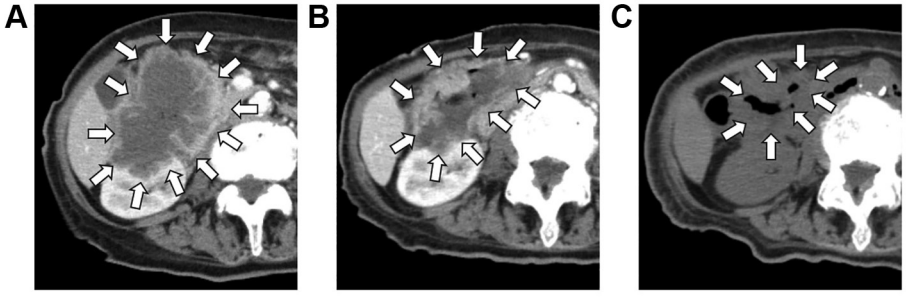

Figure 3. *Time course of abdominal computed tomography images. Abdominal computed tomography showing a large tumor (white arrows) located in the right upper abdomen before treatment (A). The size of the tumor decreased after two courses of combined CBDCA and nab-PTX therapy (B), and 10 days after the administration of larotrectinib (C). CBDCA: Carboplatin; nab-PTX: nab-paclitaxel.*

an adenocarcinoma. An immunohistochemical analysis was positive for CK 7, negative for CK20, and slightly positive for CDX2 (Figure 2). These findings appeared atypical for colon cancer. Although colorectal cancer was the most suspected diagnosis based on imaging examination, the patient was still diagnosed with CUP and initiated standard chemotherapy for CUP consisting of carboplatin (CBDCA) and nab-paclitaxel (nab-PTX). Before chemotherapy, her tumor markers were significantly elevated (CEA, 22.3 ng/ml; CA 19-9, 4554 U/ml) and the tumor increased in size (Figure 3A). After two cycles of chemotherapy, the tumor demonstrated a partial response with a reduction in size (Figure 3B) and a decrease in tumor markers (CEA, 13.1 ng/ml; CA 19-9, 3726 U/ml). However, the patient experienced significant adverse effects, including fatigue and anorexia. CGP was further explored to determine potential genetic alterations using OncoGuide™ NCC Oncopanel System (Sysmex, Hyogo, Japan) and revealed several key mutations: a tumor mutation burden (TMB) of 100 mutations per megabase (Mb), microsatellite instability-high (MSI-high, MSI score: 60.35) status, *TPM3-NTRK1* fusion gene (Figure 4), and various somatic mutations (Table I, Table II). Based

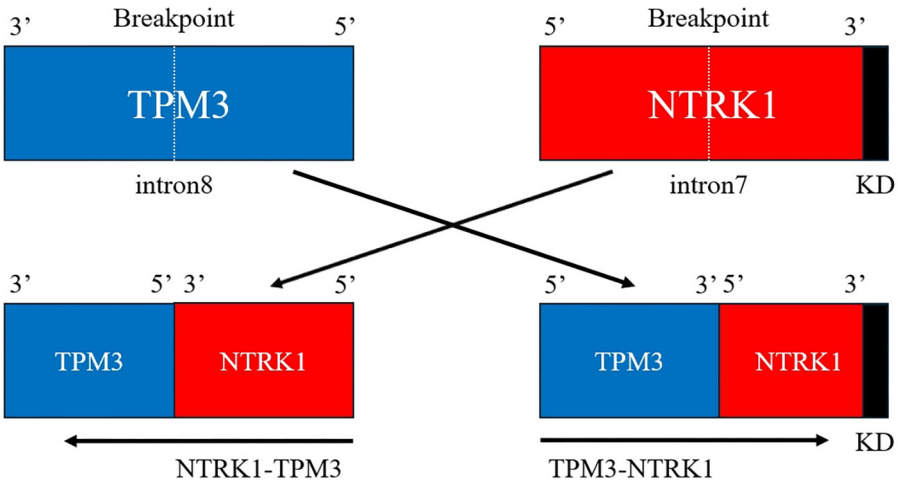

Figure 4. *Schematic representation of TPM3-NTRK1 genomic DNA breakpoints. TPM3-NTRK1 and NTRK1-TPM3 are produced as the result of an inversion on the long arm of chromosome 1. Breakpoints for TPM3 and NTRK1 are intron8 and intron7, respectively. TPM3-NTRK1 contains the N-terminal sequence of TPM3 fused with the C-terminal sequence of NTRK1 including the kinase domain (bottom right), whereas NTRK1-TPM3 lacks the kinase domain of NTRK1 (bottom left). TPM3: Tropomyosin 3; NTRK1: neurotrophic tropomyosin receptor tyrosine kinase 1; KD: kinase domain.*

on CGP results, the candidates of treatment could be an immune checkpoint inhibitor, pembrolizumab, and TRK inhibitors such as larotrectinib.

Considering the superior therapeutic efficacy of larotrectinib for NTRK1 fusions compared to pembrolizumab for MSI-high and/or high tumor mutation burden in clinical trials (4, 5), we selected larotrectinib. CT was performed ten days after starting treatment with larotrectinib, and the therapeutic response was assessed as partial response (maximum tumor diameter from 57.9 to 40.1mm, 31% reduction) according to Response Evaluation Criteria in Solid Tumors (RECIST) v1.1 (Figure 3C). Unfortunately, the patient developed acute respiratory distress eleven days after the initiation of larotrectinib and subsequently died. As the family declined an autopsy, the exact cause of death remains unknown.

Discussion

CUP accounts for approximately 3%-5% of all cancers (1). CUP is a heterogeneous group of cancers, and its prognosis varies depending on the subtype and genetic characteristics of the disease. Approximately 80% of CUP cases are classified as having a poor prognosis. In general, CUP is found at a highly advanced stage, including in distant and multiple metastases. Therefore, the primary treatment tends to rely on chemotherapy. Chemotherapy regimens for CUP are typically determined based on histopathological features and presumed site of origin. Platinum-based or taxane-based chemotherapy is commonly used. In recent years, immune checkpoint inhibitors such as nivolumab have also been introduced (6). However, the prognosis of CUP is poor and there has been no improvement in outcomes.

In recent years, the advent of CGP using NGS has revolutionized the management of cancer treatments with poor prognosis (7). NGS detects actionable genetic mutations with greater accuracy than conventional methods such as immunohistochemistry, enabling personalized treatment strategies (2). Previous studies have reported that CGP identified genetic alterations in up to 85% of patients with CUP, and that 13% to 64% of these patients may benefit from currently available targeted therapies (8). Another report indicated that frequently detected alterations in CUP include mutations in erb-b2 receptor tyrosine kinase 2 (*ERBB2)* (7.3%), phosphatidylinositol-4,5-bisphosphate 3-kinase catalytic

Table I. *Comprehensive genomic profiling results.*

Genetic mutations	
Tumor mutation burden	100/Mb
MSI score	60.35 (High)*
TPM3|NTRK1 intron8|intron7	Present

MSI: Microsatellite instability; TPM3: tropomyosin 3; NTRK1: neurotrophic tropomyosin receptor tyrosine kinase 1. *MSI-high is defined as ≥30.

Table II. *Somatic mutations determined by CGP.*

Somatic mutation	Mutant allele frequency
PTEN N323fs*21	41.0%
CDKN2A A102V	32.2%
FGFR3 V555M	31.4%
BRCA2 T3033fs*11	28.5%
RB1 R418fs*9	27.5%
DDR2 R752C	27.5%
ATM R457*	27.5%
ARID2 S990L	27.4%
ATM c.4909+2T>C	24.5%
RB1 V654fs*4	11.3%
MAP2K4 G14fs*27	11.2%

CGP: Comprehensive genomic profiling; PTEN: phosphatase and tensin homolog; CDKN2A: cyclin-dependent kinase inhibitor 2A; FGFR3: fibroblast growth factor receptor 3; BRCA2: breast cancer susceptibility gene 2; RB1: retinoblastoma 1; DDR2: discoidin domain receptor 2; ATM: ataxia telangiectasia mutated; ARID2: AT-rich interaction domain 2; MAP2K4: mitogen-activated protein kinase kinase 4.

subunit alpha (*PIK3CA)* (6.3%), neurofibromatosis type 1 (*NF1)* (5.6%), neurofibromatosis type 2 (*NF2*) (4.6%), B-Raf proto-oncogene, serine/threonine kinase (*BRAF)* (4.3%), isocitrate dehydrogenase *1 (IDH1)* (3.3%), phosphatase and tensin homolog deleted from chromosome *(PTEN)*, fibroblast growth factor receptor 2 (*FGFR2)*, epidermal growth factor receptor (*EGFR)* (3.6% each), mesenchymal-to-epithelial transition *(MET)* (4.3%), cyclin-dependent kinase 6 (*CDK6)* (3.0%), F-Box and WD repeat domain containing 7 (*FBXW7)*, cyclin-dependent kinase 4 (*CDK4)* (2.3% each), isocitrate dehydrogenase 2 (*IDH2),* rearranged during transfection *(RET),* c-ros oncogene 1 *(ROS1),* neurotrophic tyrosine receptor kinase *(NTRK)* (1.0% each), and anaplastic lymphoma kinase (*ALK)* (0.7%). (9). In this case, CGP revealed various genetic abnormalities, including an *NTRK* fusion gene, which enabled us to select an effective treatment with larotrectinib. As a result of targeted therapy for *NTRK* fusion using larotrectinib, the patient achieved a partial response. This illustrates the potential benefits of CGP in CUP, where traditional approaches may not provide sufficient information for treatment decisions. Although there have been reports of extremely poor outcomes in pancreatic cancer cases harboring PTEN mutations (10), our case, despite the presence of a PTEN mutation, demonstrated a favorable response to treatment.

The *NTRK* gene encodes tropomyosin receptor kinase (TRK), which is involved in the differentiation and survival of nerve cells (11). It has been reported that *TPM3-NTRK1* and *NTRK1-TPM3* are produced as the result of an inversion in the long arm of chromosome 1, shown in Figure 4. TPM3–NTRK1 consists of the 5′-terminal sequences of TPM3 fused to the 3′-terminal sequences of NTRK1. (4). Therefore, *TPM3-NTRK1* has been recognized as a pathological variant. *NTRK1* plays a central role in activating TRK fusion proteins, which in turn activate a signaling pathway that promotes cell proliferation and survival (11).

The primary lesion in this case was first suspected to be colon cancer because a tumor lesion was observed around the transverse colon of the hepatic flexure on CT. An endoscopic examination showed no mucosal changes, and the immunohistochemistry results were inconsistent with those of typical colon cancer, leading to a diagnosis of CUP. However, considering that the tumor was confined to the hepatic flexure and that no other metastatic lesions were identified, this case is better regarded as an unknown primary gastrointestinal tumor rather than carcinoma of unknown primary origin. We considered a colorectal origin to be the most likely, based on the following three reasons.

The first reason is that a previous study reported that *NTRK* fusion genes are highly prevalent (>90%) in salivary gland and breast secretory carcinomas (12). However, their occurrence in gastrointestinal tumors,

such as colon and gastric cancers, is reported to be extremely low (<1%). Likewise, MSI-high status is seen in only 3.78% of colon cancers (13). However, sporadic MSI-high colorectal cancers (CRC) are known to harbor a higher rate of complex genetic rearrangements, including targetable fusions such as *NTRK* (12). A previous study found that the rate of tumors being both *NTRK*-positive and MSI-high was only 0.93% in non-CRC tumors, while the rate rose sharply to 61.8% in CRC cases. In our case, the tumor was both *NTRK*-positive and MSI-high, making colorectal cancer a plausible primary origin, despite the diagnosis of CUP.

The second reason involves the immunohistochemical profile, particularly the loss of CK20 and CDX2 expression in MSI-high tumors. In adenocarcinomas, CK7, CK20, and CDX2 staining patterns help identify the site of origin. Colorectal adenocarcinomas typically present with CK7-negative, CK20-positive, and CDX2-positive patterns. However, the tumor in this case showed an atypical profile, it was positive for CK7, negative for CK20, and slightly positive for CDX2. This combination is rare in colorectal cancer, occurring in only about 0.9% of cases according to previous reports (14). However, MSI-high tumors are known to demonstrate reduced CK20 and CDX2 expression in comparison to microsatellite stable (MSS) tumors. It has been suggested that MSI-high-related molecular pathways may contribute to this downregulation (15).

The third reason is that it was reported that *NTRK*-positive colon cancer tends to have a significantly higher TMB than *NTRK*-positive non-CRC (16). In the present case, the TMB was markedly elevated (100/Mb). Previous reports suggested that among solid tumors with *NTRK* fusion genes, CRC had the highest TMB at 55.1/Mb, followed by non-small cell carcinoma at 10.5/Mb, and ovarian cancer at 6.4/Mb (16). Therefore, our patient seemed to have extremely high TMB. In contrast, previous reports have suggested that colorectal cancers harboring PIK3CA mutations in the absence of KRAS, NRAS, and BRAF mutations tend to exhibit high TMB (17), however, no PIK3CA mutation was identified in the present case. Based on CGP results, possible treatment strategies could be an immune checkpoint inhibitor, pembrolizumab, and TRK inhibitors such as larotrectinib. Compared to the treatment efficacy between them, pembrolizumab showed around the low-30% of objective response rate (ORR), and 4.1 months or more of progression free survival (PFS) in the patients with MSI-high and/or high tumor mutation burden in phase II KEYNOTE-158 (4). Efficacy of larotrectinib was shown in a phase I/II study, the NAVIGATE study; ORR was 75% and median PFS was not reached. Therefore, we selected larotrectinib (4). However, it has been reported that *NTRK*-positive colorectal cancers respond less favorably to entrectinib than other tumor types (18). Therefore, pembrolizumab, an immune checkpoint inhibitor, may be a more suitable treatment option, particularly in the context of an MSI-high status. In this case, the patient died of respiratory failure during the treatment of larotrectinib. It is noteworthy that the tumor had favorable response, and this was speculated to be due to being *NTRK*-positive. However, it remains unclear that the safety of this treatment warrants further evaluation in future studies.

This case highlights the importance of recognizing that genetic alterations can lead to atypical diagnostic findings in CUP. In addition, findings on gene alterations could lead to a better treatment strategy that considers a range of potential primary sites, informed by molecular and genetic profiling.

Conclusion

We encountered a case of CUP with various genetic abnormalities, including *NTRK* positivity and MSI-high status. CUP is associated with poor prognosis. However, gene profiling can provide information that can be used to select an effective treatment, as well as determine the primary origin of CUP.

Conflicts of Interest

The Authors declare no competing interests regarding this work.

Authors' Contributions

HS and NA drafted the manuscript. MH and NA edited the manuscript. TS was involved in the treatment and follow-up of this case. YT was responsible for immunohistochemical image analysis. HI was responsible for the provision of medical images (CT scans). NK and CN contributed to the data analysis and interpretation. TS, YA, and NA revised the manuscript, provided valuable feedback and supervision, and approved the final manuscript for publication. All Authors have read and approved the final version of the manuscript.

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Artificial Intelligence (AI) Disclosure

No artificial intelligence (AI) tools, including large language models or machine learning software, were used in the preparation, analysis, or presentation of this manuscript.

References

1 Pavlidis N, Pentheroudakis G: Cancer of unknown primary site. Lancet 379(9824): 1428-1435, 2012. DOI: 10.1016/S0140-6736(11)61178-1

2 Binder C, Matthes KL, Korol D, Rohrmann S, Moch H: Cancer of unknown primary-Epidemiological trends and relevance of comprehensive genomic profiling. Cancer Med 7(9): 4814-4824, 2018. DOI: 10.1002/cam4.1689

3 Krämer A, Bochtler T, Pauli C, Shiu KK, Cook N, de Menezes JJ, Pazo-Cid RA, Losa F, Robbrecht DG, Tomášek J, Arslan C, Özgüroğlu M, Stahl M, Bigot F, Kim SY, Naito Y, Italiano A, Chalabi N, Durán-Pacheco G, Michaud C, Scarato J, Thomas M, Ross JS, Moch H, Mileshkin L: Molecularly guided therapy versus chemotherapy after disease control in unfavourable cancer of unknown primary (CUPISCO): an open-label, randomised, phase 2 study. Lancet 404(10452): 527-539, 2024. DOI: 10.1016/S0140-6736(24)00814-6

4 Maio M, Ascierto PA, Manzyuk L, Motola-Kuba D, Penel N, Cassier PA, Bariani GM, De Jesus Acosta A, Doi T, Longo F, Miller WH, Oh DY, Gottfried M, Xu L, Jin F, Norwood K, Marabelle A: Pembrolizumab in microsatellite instability high or mismatch repair deficient cancers: updated analysis from the phase II KEYNOTE-158 study. Ann Oncol 33(9): 929-938, 2022. DOI: 10.1016/j.annonc.2022.05.519

5 Drilon A, Laetsch TW, Kummar S, DuBois SG, Lassen UN, Demetri GD, Nathenson M, Doebele RC, Farago AF, Pappo AS, Turpin B, Dowlati A, Brose MS, Mascarenhas L, Federman N, Berlin J, El-Deiry WS, Baik C, Deeken J, Boni V, Nagasubramanian R, Taylor M, Rudzinski ER, Meric-Bernstam F, Sohal DPS, Ma PC, Raez LE, Hechtman JF, Benayed R, Ladanyi M, Tuch BB, Ebata K, Cruickshank S, Ku NC, Cox MC, Hawkins DS, Hong DS, Hyman DM: Efficacy of larotrectinib in TRK fusion-positive cancers in adults and children. N Engl J Med 378(8): 731-739, 2018. DOI: 10.1056/NEJMoa1714448

6 Tanizaki J, Yonemori K, Akiyoshi K, Minami H, Ueda H, Takiguchi Y, Miura Y, Segawa Y, Takahashi S, Iwamoto Y, Kidera Y, Fukuoka K, Ito A, Chiba Y, Sakai K, Nishio K, Nakagawa K, Hayashi H: Open-label phase II study of the efficacy of nivolumab for cancer of unknown primary. Ann Oncol 33(2): 216-226, 2022. DOI: 10.1016/j.annonc.2021.11.009

7 Aoyama R, Nishikubo H, Kawabata K, Kanei S, Yamamoto Y, Nishimura S, Yashiro M: Clinical significance of multi-cancer genome profiling: data from a single hospital in Japan. Cancer Genomics Proteomics 21(1): 79-87, 2024. DOI: 10.21873/cgp.20431

8 Limaye S, Deshmukh J, Rohatagi N, Prabhash K, Rauthan A, Singh S, Kumar A: Usefulness of comprehensive genomic profiling in clinical decision-making in oncology: a systematic review. J Immunother Precis Oncol 8(1): 55-63, 2025. DOI: 10.36401/JIPO-24-11

9 Ross JS, Sokol ES, Moch H, Mileshkin L, Baciarello G, Losa F, Beringer A, Thomas M, Elvin JA, Ngo N, Jin DX, Krämer A: Comprehensive genomic profiling of carcinoma of unknown primary origin: retrospective molecular classification considering the CUPISCO study design. Oncologist 26(3): e394-e402, 2021. DOI: 10.1002/onco.13597

10 Saito Y, Suzuki S, Sanomachi T, Kato K, Otake H, Nishise Y, Yamada Y, Saito K, Takahashi K, Kumanishi R, Fukui T, Yoshioka T: Pancreatic Mixed acinar-neuroendocrine carcinoma in a patient with a germline PTEN variant: a case report and genomic literature review. In Vivo 39(2): 1173-1181, 2025. DOI: 10.21873/invivo.13921

11 Ardini E, Bosotti R, Borgia AL, De Ponti C, Somaschini A, Cammarota R, Amboldi N, Raddrizzani L, Milani A, Magnaghi P, Ballinari D, Casero D, Gasparri F, Banfi P, Avanzi N, Saccardo MB, Alzani R, Bandiera T, Felder E, Donati D, Pesenti E, Sartore-Bianchi A, Gambacorta M, Pierotti MA, Siena S, Veronese S, Galvani A, Isacchi A: The TPM3-NTRK1 rearrangement is a recurring event in colorectal carcinoma and is associated with tumor sensitivity to TRKA kinase inhibition. Mol Oncol 8(8): 1495-1507, 2014. DOI: 10.1016/j.molonc.2014.06.001

12 Westphalen CB, Krebs MG, Le Tourneau C, Sokol ES, Maund SL, Wilson TR, Jin DX, Newberg JY, Fabrizio D, Veronese L, Thomas M, de Braud F: Genomic context of NTRK1/2/3 fusion-positive tumours from a large real-world population. NPJ Precis Oncol 5(1): 69, 2021. DOI: 10.1038/s41698-021-00206-y
13 Akagi K, Oki E, Taniguchi H, Nakatani K, Aoki D, Kuwata T, Yoshino T: Real-world data on microsatellite instability status in various unresectable or metastatic solid tumors. Cancer Sci 112(3): 1105-1113, 2021. DOI: 10.1111/cas.14798
14 Dum D, Menz A, Völkel C, De Wispelaere N, Hinsch A, Gorbokon N, Lennartz M, Luebke AM, Hube-Magg C, Kluth M, Fraune C, Möller K, Bernreuther C, Lebok P, Clauditz TS, Jacobsen F, Sauter G, Uhlig R, Wilczak W, Steurer S, Minner S, Marx AH, Simon R, Burandt E, Krech T: Cytokeratin 7 and cytokeratin 20 expression in cancer: A tissue microarray study on 15,424 cancers. Exp Mol Pathol 126: 104762, 2022. DOI: 10.1016/j.yexmp.2022.104762
15 Olsen J, Eiholm S, Kirkeby LT, Espersen ML, Jess P, Gögenür I, Olsen J, Troelsen JT: CDX2 downregulation is associated with poor differentiation and MMR deficiency in colon cancer. Exp Mol Pathol 100(1): 59-66, 2016. DOI: 10.1016/j.yexmp.2015.11.009
16 Arter ZL, Lee ATM, Nagasaka M, Ou SI: Tumor mutation burden survey of AACR GENIE database revealed NTRK (NTRK+) and RET (RET+) fusions positive colorectal carcinoma (CRC) as distinct subsets. Cancer Med 14(4): e70665, 2025. DOI: 10.1002/cam4.70665
17 Voutsadakis IA: PIK3CA mutated colorectal cancers without KRAS, NRAS and BRAF mutations possess common and potentially targetable mutations in epigenetic modifiers and DNA damage response genes. Cancer Genomics Proteomics 21(5): 533-548, 2024. DOI: 10.21873/cgp.20470
18 Demetri GD, De Braud F, Drilon A, Siena S, Patel MR, Cho BC, Liu SV, Ahn MJ, Chiu CH, Lin JJ, Goto K, Lee J, Bazhenova L, John T, Fakih M, Chawla SP, Dziadziuszko R, Seto T, Heinzmann S, Pitcher B, Chen D, Wilson TR, Rolfo C: Updated integrated analysis of the efficacy and safety of entrectinib in patients with NTRK fusion-positive solid tumors. Clin Cancer Res 28(7): 1302-1312, 2022. DOI: 10.1158/1078-0432.CCR-21-3597