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ASCO 2025

Top Breakthroughs & Publications Shared

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Breast Cancer

- *INAVO120 phase III trial: New triple therapy for aggressive, advanced breast cancer slows the progression of the disease, delays the need for further chemotherapy.*
  - The trial evaluated the addition of inavolisib to palbociclib and fulvestrant in patients with PIK3CA-mutated, HR+/HER2- endocrine-resistant advanced breast cancer
  - Primary endpoint was met with statistically significant improvement in progression-free survival. Median PFS was 17.2 months with inavolisib versus 7.3 months with placebo (HR 0.42; 95% CI, 0.32–0.55), and overall survival was also significantly prolonged at 34.0 months versus 27.0 months (HR 0.67; 95% CI, 0.48–0.94).
  - The inavolisib arm showed a higher objective response rate (62.7% vs. 28.0%) and more than doubled the median time to chemotherapy (35.6 months vs. 12.6 months), supporting its clinical impact on delaying disease progression and treatment escalation.
  - Safety findings were consistent with known profiles, with common grade ≥3 adverse events including hyperglycemia, neutropenia, and diarrhea; no new safety signals were identified.
  - These results confirm inavolisib's potential to be a practice-changing addition to first-line treatment in this genetically defined population.

https://meetings.asco.org/abstracts-presentations/244382

- *Sacituzumab govitecan (SG) + pembrolizumab in unresectable locally advanced/metastatic PD-L1-positive triple-negative breast cancer (Phase 3 ASCENT-04/KEYNOTE-D19 study – primary results).*
  - After a median follow-up of 14 months, patients treated with sacituzumab govitecan and pembrolizumab (n=221) had a progression-free survival of 11.2 months vs. 7.8 months in the chemotherapy and pembrolizumab arm (n=222).
  - Median duration of response was 16.5 months for the sacituzumab govitecan and pembrolizumab arm vs. 9.2 months for the chemotherapy and pembrolizumab arm.

- The most frequent grade 3 and 4 adverse events in the sacituzumab govitecan and pembrolizumab arm were neutropenia (43%) and diarrhea (10%). In the chemotherapy and pembrolizumab arm, the most frequent grade 3 and 4 adverse events were neutropenia (45%), anemia (16%), and thrombocytopenia (14%).
- Researchers will continue to follow these patients to better understand if there is an overall survival benefit for patients treated with sacituzumab govitecan and pembrolizumab compared to the control group. This drug combination is also being studied in patients with human epidermal growth factor receptor (HER2)-negative metastatic breast cancer, early-stage TNBC, and hormone receptor-positive/HER2-negative metastatic breast cancer after hormone therapy.

https://meetings.asco.org/abstracts-presentations/253362

- *Trastuzumab deruxtecan (T-DXd) + pertuzumab (P) vs taxane + trastuzumab + pertuzumab (THP) for first-line treatment of patients HER2+ advanced/metastatic breast cancer - Interim results from DESTINY-Breast09 (phase 3).*
  - 1,157 total patients, 770 of whom were randomized to receive either trastuzumab deruxtecan with pertuzumab (383 patients) or the current standard of care (387 patients) reported a current median follow-up of nearly 2.5 years (29 months).
  - Trastuzumab deruxtecan with pertuzumab reduced the risk of disease progression or death by 44% for patients. The median progression-free survival (PFS) was 40.7 months in the trastuzumab deruxtecan with pertuzumab group versus 26.9 months In the THP group. This benefit was seen across all subgroups.
  - At 2 years, about 70% of patients in the trastuzumab deruxtecan with pertuzumab group had not seen their cancer grow or spread, compared to about 52% in the THP group.
  - For the patients who received trastuzumab deruxtecan and pertuzumab, about 85% had their cancer shrink or disappear compared to 78.6% of those in the THP group. About 15% of patients who responded to treatment with

trastuzumab deruxtecan and pertuzumab had no signs of cancer in response to the treatment vs. 8.5% in the THP group.

- The analysis of overall survival is immature, but researchers observed a trend in improvement in overall survival for those in the trastuzumab deruxtecan with pertuzumab group.
- Both groups experienced similar rates of serious side effects. However, the length of treatment was longer in the trastuzumab deruxtecan group, and certain side effects—including nausea, vomiting, and constipation—were more common in this group. Interstitial lung disease, a known side effect of trastuzumab deruxtecan, occurred in about 12% of patients in this group with most cases not severe.

https://meetings.asco.org/abstracts-presentations/253126

- *Use of artificial intelligence–assistance software for HER2-low and HER2-ultralow IHC interpretation training to improve diagnostic accuracy of pathologists and expand patients' eligibility for HER2-targeted treatment.*
  - The study addresses the challenge of accurately identifying HER2-low and HER2-ultralow breast cancers, which is crucial for determining eligibility for HER2-targeted therapies. To enhance diagnostic precision, researchers developed and implemented an artificial intelligence (AI)–assistance software aimed at improving pathologists' interpretation of HER2 immunohistochemistry (IHC) results.
  - Pathologists underwent training with the AI-assisted software. The AI tool provided real-time feedback and standardized scoring, leading to more consistent and reliable HER2 status assessments across different observers.
  - AI-assisted training improved pathologists' accuracy in HER2 IHC scoring by 13.3%, compared to central reference scores. Furthermore, AI reduced the misclassification of HER2-low and HER2-ultralow cases as HER2 null by 25.5%, potentially enabling more patients to access HER2-targeted therapies.
  - The study concludes that integrating AI-assisted training into pathology workflows can substantially improve the accuracy and reduce inter-observer variability of HER2 IHC interpretation. This advancement has the potential to

expand patient access to HER2-targeted treatments, ultimately improving clinical outcomes for individuals with breast cancer.

https://ascopubs.org/doi/10.1200/JCO.2025.43.16_suppl.1014

Prostate Cancer

- *Multimodal artificial intelligence (MMAI) model to identify benefit from 2nd-generation androgen receptor pathway inhibitors (ARPI) in high-risk non-metastatic prostate cancer patients.*
  - The study developed a multimodal AI model using digitized histopathology from over 2,000 STAMPEDE trial patients to predict which men with high-risk non-metastatic prostate cancer benefit from adding abiraterone to ADT.
  - In a validation group of 788 patients, the model identified a high-benefit group where 5-year OS improved from 71% to 85% with abiraterone (HR 0.40, p=0.00014).
  - In the low-benefit group, the 5-year OS gain was smaller and not statistically significant—80% to 85% (HR 0.77, p=0.25).
  - Model predictions were independent of clinical factors like Gleason score and validated in a Canadian cohort.
  - About 40% of men may gain real OS benefit from abiraterone, helping target treatment while avoiding unnecessary toxicity in others.

https://ascopubs.org/doi/10.1200/JCO.2025.43.16_suppl.5001

Lung Cancer

- *Lurbinectedin + atezolizumab as first-line maintenance treatment in patients with extensive-stage small cell lung cancer (Phase 3 IMforte trial - primary results).*
  - After a median follow-up of 15 months, the median progression-free survival (PFS) was 5.4 months in the lurbinectedin and atezolizumab arm versus 2.1 months in the atezolizumab alone arm (stratified HR, 0.54 [95% CI: 0.43, 0.67]; $P<0.0001$).

- The median overall survival was 13.2 months for patients treated with lurbinectedin and atezolizumab and 10.6 months for patients treated with atezolizumab alone (stratified HR, 0.73 [95% CI: 0.57, 0.95]; *P*=0.0174).
- There was a noted difference in adverse events between the two groups. Treatment-related adverse events occurred in 83.5% of patients in the lurbinectedin and atezolizumab arm, compared to 40% in the atezolizumab alone arm. In the lurbinectedin and atezolizumab arm, 25.6% of patients experienced a grade 3 or 4 adverse event and 0.8% experienced a grade 5 adverse event. In the atezolizumab alone arm, 5.8% experienced a grade 3 or 4 adverse event and 0.4% experienced a grade 5 adverse event. In the lurbinectedin and atezolizumab arm, 6.2% of patients stopped treatment due to side effects compared to 3.3% in the atezolizumab alone arm.

https://meetings.asco.org/abstracts-presentations/243670

Melanoma

- *Long-term Efficacy and Safety of Lifileucel Tumor-infiltrating Lymphocyte (TIL) Cell Therapy in Patients with Advanced Melanoma: A 5-year Analysis of the C-144-01 Study.*
  - One of the largest and longest prospective studies in ICI-refractory advanced melanoma assessed lifileucel, an autologous TIL therapy. In 153 patients with unresectable/metastatic melanoma who progressed after anti–PD-1/PD-L1 and BRAF/MEK inhibitors, a single lifileucel infusion was administered following lymphodepletion and IL-2. Outcomes were tracked over 5 years.
  - The 5-year objective response rate (ORR) was 31.4%, including 5.9% complete responses (CR) and 25.5% partial responses (PR), with a median time to response of 1.4 months. Tumor burden was reduced in 79.3% of patients. Sixteen patients showed deepened responses, with four converting from PR to CR over a year after infusion. Among responders, 31.3% had ongoing responses at year five, and the median duration of response was 36.5 months.
  - Median overall survival (OS) was 13.9 months, and the 5-year OS rate was 19.7%, notable in this heavily pretreated group. Subgroup analysis showed

improved outcomes in patients with lower tumor burden and fewer brain/liver metastases. No significant OS differences were found between early and late responders or those with deepened responses.

- Safety was consistent with expected effects of lymphodepletion and IL-2. Most grade 3/4 cytopenias resolved to grade ≤2 within 30 days. Adverse events declined within two weeks. Fatal treatment-related events occurred in 3.2% of patients, primarily within 30 days and linked to the preparative regimen.
- This 5-year analysis supports lifileucel's durable efficacy and manageable safety as a one-time treatment in advanced melanoma, especially after checkpoint inhibitor and targeted therapy failure, reinforcing its value in treatment strategies.

https://ascopubs.org/doi/pdf/10.1200/JCO-25-00765

Gastrointestinal Cancers

- *Romiplostim for chemotherapy-induced thrombocytopenia (CIT) in colorectal, gastroesophageal, and pancreatic cancers (global phase 3 RCT).*
  - This randomized phase 3 trial evaluated romiplostim in patients with chemotherapy-induced thrombocytopenia (CIT) from gastrointestinal cancers
  - The study demonstrated a significantly higher primary endpoint achievement with romiplostim (84%) compared to placebo (36%), with an odds ratio of 10.2 (95% CI 4.6–22.5; P<0.001). Median platelet nadirs were higher in the romiplostim group (87×10^9/L) versus placebo (58×10^9/L; P=0.005). Among responders, the median time to platelet response was shorter with romiplostim at 1.1 weeks compared to 2.1 weeks for placebo (P<0.001).
  - Romiplostim group maintained higher relative dose intensity of chemotherapy, suggesting that the treatment allowed patients to adhere more closely to their prescribed chemotherapy regimens without the need for dose reductions or delays.
  - Safety profiles were comparable between the two groups (adverse effects in 12% of romiplostim patients and 7% of placebo patients), with no treatment-related serious adverse events or deaths reported.

- Robust evidence supporting the use of romiplostim as an effective and safe intervention for managing CIT in patients with gastrointestinal cancers, potentially improving chemotherapy adherence and patient outcomes.

https://ascopubs.org/doi/10.1200/JCO.2025.43.16_suppl.12007

- *First-line encorafenib + cetuximab + mFOLFOX6 in BRAF V600E-mutant metastatic colorectal cancer (BREAKWATER): Progression-free survival and updated overall survival analyses.*
  - The study originally included three treatment arms: encorafenib/cetuximab alone (158 patients), encorafenib/cetuximab with mFOLFOX6 (236 patients), and the control arm of chemotherapy with or without bevacizumab (243 patients).
  - When early results showed that the encorafenib/cetuximab with mFOLFOX6 arm had a statistically significant improvement in objective response rates (ORR), enrollment in the encorafenib/cetuximab alone arm was closed in a protocol amendment.
  - Overall survival was 30.3 months in the encorafenib/cetuximab with mFOLFOX6 arm, 19.5 months in the encorafenib/cetuximab alone arm, and 15.1 months in the control arm. Patients treated with encorafenib/cetuximab with mFOLFOX6 had a 51% lower risk of dying than patients treated with the standard of care chemotherapy with or without bevacizumab.
  - Progression-free survival was 12.8 months in the encorafenib/cetuximab plus mFOLFOX6 arm, 6.8 months in the encorafenib/cetuximab alone arm, and 7.1 months in the control arm.
  - Most of the side effects for these treatments were manageable. Serious side effects caused by the treatments occurred in 30% of patients in the encorafenib/cetuximab alone arm, 46% of the encorafenib/cetuximab with mFOLFOX6 arm, and 39% of the control arm. The most common side effects for the encorafenib/cetuximab with mFOLFOX6 treatment were nausea, anemia, and diarrhea.

https://meetings.asco.org/abstracts-presentations/243633

- *Pivotal phase 2 trial evaluating satricabtagene autoleucel (satri-cel), an autologous CLDN18.2-specific chimeric antigen receptor (CAR) T-cell therapy, in patients with advanced gastric or gastro-oesophageal junction cancer.*
  - The study enrolled patients with advanced gastric or gastro-oesophageal junction cancer who had previously received at least two lines of systemic therapy. Participants underwent leukapheresis for T-cell collection, followed by lymphodepleting chemotherapy and a single infusion of satri-cel.
  - Results demonstrated a confirmed ORR of 57.1%, with a median PFS of 5.6 months and a median OS of 10.8 months. Notably, patients with high CLDN18.2 expression exhibited an ORR of 61.1%. The therapy's efficacy was consistent across various subgroups, including those with peritoneal metastases and prior exposure to anti-PD-1 therapy.
  - Regarding safety, the most common grade 3 or higher adverse events were hematologic toxicities, including neutropenia (85.7%), leukopenia (71.4%), and anemia (42.9%). Cytokine release syndrome occurred in 85.7% of patients, predominantly grade 1 or 2, with only one patient experiencing grade 3. No treatment-related deaths were reported.
  - In conclusion, satri-cel demonstrated promising antitumor activity and a manageable safety profile in heavily pretreated patients with advanced gastric or gastro-oesophageal junction cancer.

https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(25)00860-8/fulltext

- *First prospective phase 2 trial challenging the immediate-surgery paradigm in esophageal cancer*
  - In this trial, patients who were non-complete responders after CRT received additional chemotherapy combined with immunotherapy before proceeding to surgery. The results demonstrated that this sequential approach led to improved pathological response rates compared to historical controls who underwent immediate surgery post-CRT.
  - The study included 87 non-complete clinical responders, with 54 receiving sequential chemo-immunotherapy (SCI) and 33 undergoing direct surgery (DS),

with most patients (83.9%) at stage IIIB. In the intention-to-treat population, SCI significantly improved pathological complete response (pCR) rates (40.7% vs. 18.1%; OR 3.06, p = 0.024) and showed a trend toward higher major pathological response (MPR) rates.

- At 12 months, progression-free survival favored SCI in both ITT (95.6% vs. 77.3%) and PP populations (97.4% vs. 77.8%).
- Adverse events in the SCI group were mostly hematologic, with a few immune-related events in non-surgical patients. Postoperative complications were comparable between groups, and no severe treatment-related adverse events occurred in the SCI group.
- The study concludes that implementing a sequential chemo-immunotherapy regimen for non-complete responders after neoadjuvant CRT may enhance treatment outcomes and offers a promising alternative to immediate surgery in esophageal cancer management.

https://ascopubs.org/doi/10.1200/JCO.2025.43.16_suppl.4066

https://www.clinicaltrials.gov/study/NCT05189730

Gynecological Cancers

- *Phase II dose optimization update with EZH2/EZH1 inhibitor tulmimetostat in patients with ARID1A-mutated ovarian clear cell carcinoma (OCCC) or endometrial carcinoma. (EC)*
  - The study used a two-stage dose-optimization design to compare 200 mg, 300 mg, and 350 mg daily doses, with efficacy and safety endpoints across the M2 (OCCC, n=54) and M3 (EC, n=36) cohorts.
  - Most antitumor activity was observed in the M2 200 mg and M3 350 mg groups (n=20;n=14), each showing four confirmed responses. A majority of participants (56.4% in M2 and 61.9% in M3) had previously undergone at least three lines of therapy, indicating a heavily pretreated population.
  - The trial also documented that treatment-emergent adverse events (TEAEs) led to dose modifications in over half of the patients, with higher rates observed at the 350 mg dose, particularly in the EC cohort.

- Serious treatment-related adverse events (TRAEs), mainly hematologic in nature, occurred more frequently with increasing doses, although no deaths were attributed to the drug. Discontinuations due to TEAEs were less common at the 200 mg and 300 mg doses compared to the 350 mg cohort.

https://meetings.asco.org/abstracts-presentations/249366

Head and Neck Cancer

- *Addition of Perioperative Pembrolizumab to Standard of Care in Newly Diagnosed Locally Advanced Head and Neck Cancer*
  - The KEYNOTE-689 trial evaluated the addition of neoadjuvant and adjuvant pembrolizumab to standard radiotherapy with or without chemotherapy in locally advanced head and neck cancer.
  - Perioperative pembrolizumab significantly improved event-free survival, reducing the risk by 37% among patients with a combined positive score ≥ 10 and improving the odds of achieving a major pathologic response.
  - This is the first significant treatment advance in the previously untreated, locally advanced setting for this this malignancy in decades.
  - Full results are not available the trial is still on-going; these results are based on median follow-up of 38.3 months of 714 patients with stage III or IVA newly diagnosed respectable head and neck squamous cell carcinoma.

https://ascopost.com/issues/may-10-2025/addition-of-perioperative-pembrolizumab-to-standard-of-care-in-newly-diagnosed-locally-advanced-head-and-neck-cancer/
https://clinicaltrials.gov/study/NCT03765918

Novel Treatments

- *First-in-human phase I/II trial evaluating BNT142, a first-in-class mRNA encoded, bispecific antibody targeting Claudin 6 (CLDN6) and CD3, in patients (pts) with CLDN6-positive advanced solid tumors.*
  - The BNT142-01 trial is a multi-center study, this initial report presents results from the dose escalation stage, where patients received one of seven dose

levels of weekly intravenous BNT142, with safety, tolerability, pharmacokinetics, and early efficacy as primary and secondary endpoints.

- The study enrolled 65 patients with various cancers, most commonly ovarian, and 71% had received at least four prior systemic treatments.
- Adverse events related to BNT142 were mostly mild to moderate, with 23% experiencing grade 3 or higher treatment-related adverse events, primarily cytokine release syndrome and elevated liver enzymes.
- BNT142 induced transient inflammatory cytokine responses and showed a disease control rate of 58% across all dose levels, with better responses at higher doses. Among ovarian cancer patients, seven achieved partial responses per RECIST 1.1, and the disease control rate reached 75%, suggesting dose-related clinical activity.
- In conclusion, BNT142 showed a tolerable safety profile and promising early efficacy, particularly in ovarian cancer, supporting further dose optimization. These results offer the first clinical validation for an mRNA-encoded bispecific antibody therapeutic.

https://meetings.asco.org/abstracts-presentations/244343

- *Preliminary results from a first-in-human, phase I/II study of VLS-1488, an oral KIF18A inhibitor in patients with advanced solid tumors.*
  - The trial investigated the oral KIF18A inhibitor VLS-1488 in patients with advanced solid tumors, particularly those characterized by chromosomal instability (CIN). The study began with a dose-escalation phase to determine the Maximum Tolerated Dose (MTD), followed by an expansion phase. All patients had measurable disease and were previously treated with multiple lines of therapy.
  - Among the 52 patients treated across five dose levels (50 to 800 mg), treatment-related adverse events occurred in 42% of patients, most commonly fatigue (17.3%), elevated AST (13.5%), and rash (11.5%), with only 12% experiencing grade 3 toxicities and none above grade 3.
  - Efficacy analyses included 41 evaluable patients, with particular benefit noted in high-grade serous ovarian cancer (HGSOC) patients. Of the 16 evaluable

HGSOC patients, 3 achieved partial responses—2 of which were durable over 24 weeks—and 6 had stable disease, including tumor reductions, across various dose levels. Five patients remained on treatment at the time of data cutoff.

- The study concluded that VLS-1488 demonstrates a favorable safety profile and encouraging early signs of anti-tumor activity, especially in heavily pretreated HGSOC patients, warranting further evaluation in the ongoing Dose Expansion phase.

https://meetings.asco.org/abstracts-presentations/246279

Lifestyle & Supportive Care

- *Structured Exercise Program Improves Survival, Outcomes in Some Patients With Colon Cancer.*
  - The CHALLENGE trial, a phase III randomized study, evaluated whether a 3-year structured exercise program improves disease-free survival (DFS) compared to health education in 962 patients with stage III or high-risk stage II colon cancer who completed adjuvant chemotherapy.
  - **The trial did not meet its primary endpoint; structured exercise did not significantly improve DFS compared to health education after a median follow-up of 7.5 years.**
  - However, a prespecified subgroup analysis revealed that patients with a body mass index (BMI) under 25 derived a statistically significant DFS benefit from the exercise program, suggesting differential effects based on baseline patient characteristics.
  - While exercise did not universally improve DFS, secondary outcomes such as quality of life and physical fitness may still support its use as a complementary component in post-treatment cancer care.

https://meetings.asco.org/abstracts-presentations/244420

- *Effect of glucagon-like peptide-1 (GLP-1) receptor agonists on risk of fourteen obesity-related cancers*

- In the GLP-1 receptor agonist group, there were 2,501 newly diagnosed cases of obesity-related cancer out of 85,015. In the DDP-4 inhibitor group, there were 2,671 cases of obesity-related cancer out of 85,015.
- Over a mean follow-up of 3.9 years, there was a lower risk of obesity-related cancers (adjusted HR, 0.93; 95% CI, 0.88-0.98; P=0.005) and all-cause death (adjusted HR, 0.92; 95% CI 0.87-0.97; P=0.001) associated with GLP-1RA use versus DPP-4i use.
- With no statistical significance between the groups in men, whilw women in the GLP-1 arm had an 8% lower risk of obesity-related cancer (p=0.01) and a 20% lower risk of all causes of death compared to women in the DDP-4 arm (p<0.001).
- Assessments of cancer subtypes showed protective associations between GLP-1RA use and colon and rectal cancers.

https://meetings.asco.org/abstracts-presentations/246442

Liquid Biopsy (Lung and Breast Cancer)

- *ctDNA-Guided Treatment Switch to Camizestrant Before Clinical Progression Improves Outcomes in ESR1-Mutated, HR-Positive/HER2-Negative Advanced Breast Cancer.*
  - The SERENA-6 trial demonstrated that switching to camizestrant, an oral selective estrogen receptor degrader (SERD), at the time of rising ctDNA—before clinical progression—significantly delayed disease progression in patients with ER-positive, HER2-negative advanced breast cancer receiving first-line aromatase inhibitor and CDK4/6 inhibitor therapy.
  - 315 eligible patients were randomized to either switch to camizestrant (n=157) or continue with aromatase inhibitor therapy (n=158), with approximately 50% showing ESR1 mutations at their first ctDNA test. Following 171 progression-free survival (PFS) events, camizestrant significantly reduced the risk of progression with a hazard ratio of 0.44, extending median PFS to 16.0 months compared to 9.2 months with continued AI therapy. The hazard ratio for PFS2 was 0.52 (95%

CI: 0.33–0.81) at 27% maturity, while overall survival data remain immature with 12% maturity.

- The trial validates the concept of molecular progression as a therapeutic trigger, suggesting that ctDNA surveillance can be used not only to monitor disease but also to proactively guide treatment changes in a clinically meaningful way.
- Camizestrant was generally well tolerated, with a safety profile consistent with earlier trials and no new unexpected adverse events reported, supporting its use in early intervention strategies.

https://dailynews.ascopubs.org/do/serena-6-ctdna-guided-treatment-switch-camizestrant-before-clinical-progression

https://meetings.asco.org/abstracts-presentations/245971

- *NHS England is the first healthcare system in the world to implement large-scale use of liquid biopsies using circulating tumor DNA (ctDNA) for cancer patients.*
  - The ctDNA blood test accelerates diagnosis by up to 16 days compared to traditional biopsies, while also reducing the need for invasive tissue sampling. Faster results lead to quicker initiation of personalized cancer therapies.
  - The program targets 15,000 lung cancer and 5,000 advanced breast cancer patients annually, enabling tailored treatments based on individual tumor genetics. This represents a shift toward more individualized oncology care at the population level.
  - Early analysis suggests the initiative could save the NHS £11 million per year in lung cancer treatment costs alone, through more efficient care and reduced reliance on chemotherapy.
  - Future plans include expanding ctDNA testing to other cancer types such as pancreatic and gallbladder cancers, aiming to broaden access to precision oncology tools across the NHS.

https://norththamesgenomics.nhs.uk/circulating-tumour-testing-in-the-nhs/