CAPPA, a phase 2 study to evaluate capecitabine plus pembrolizumab as post-operative adjuvant therapy for triple-negative breast cancer with residual disease after neoadjuvant chemo-immunotherapy

D. Loirat[1], F. C. Bidard[1], J. Grenier[2], T. L'Haridon[3], A. Kieffer[4], F. Dalenc[5], C. Goislard De Monsabert[6], F. Ricci[7], M. By[8], D. Bello Roufai[1], Y. Kirova[9], T. Roque[10], A. Savignoni[11], J. Y. Pierga[1]

[1]Institut Curie and Institute of Women's cancers, Paris, France; [2]Institut du cancer Avignon Provence; [3]Clinique Mutualiste de l'Estuaire; [4]Institut de Cancérologie de Lorraine; [5]IUCT Oncopole; [6]CHD Vendée; [7]Clinique de La Croix du Sud; [8]CHU Bretonneau; [9]Institut Curie, Dept. of Radiation Oncology; [10]R&D Unicancer; [11]Biometrics Dept., DREH, Institut Curie.

Plain Language Summary

Why this study?

Triple-negative breast cancer (TNBC) is an aggressive type of breast cancer. Even when patients receive modern neoadjuvant treatments combining chemotherapy and immunotherapy (such as pembrolizumab), some still have residual invasive disease at the time of surgery. These patients remain at high risk of relapse.

The CAPPA study aims to evaluate whether adding capecitabine, an oral chemotherapy, to pembrolizumab as adjuvant therapy after surgery can further reduce the risk of relapse in these high-risk TNBC patients.

How this study is conducted and who can participate?

CAPPA is a **multicenter, open-label, phase II trial (NCT** NCT05973864) conducted in France.

Eligible patients are adults with TNBC and residual invasive disease after completing neoadjuvant chemo-immunotherapy including pembrolizumab.

After surgery, participants receive:

- Capecitabine (1000 mg/m² (reduced at 825mg/m² during radiotherapy) twice daily, days 1–14 of each 3-week cycle, for 8 cycles), and
- Pembrolizumab (200 mg IV every 3 weeks, for 9 cycles).
- Local radiotherapy will be performed as per standard practice if indicated.

Their outcomes will be compared with a cohort of patients who previously received pembrolizumab alone as adjuvant therapy.

The study's main objective is to assess whether adding capecitabine to pembrolizumab improves **invasive disease-free survival** (IDFS), defined as the time from surgery to the first occurrence of invasive breast cancer recurrence, a new invasive cancer, or death from any cause.

What are the study endpoints?

Patients will be followed for several years to assess:

- Invasive disease-free survival (primary endpoint)
- Distant recurrence-free survival, overall survival, and safety.
- Exploratory translational analyses of tumor and plasma biomarkers to identify factors associated with treatment response and prognosis.

Study status

Recruitment is **ongoing**. The first patient was enrolled in March 2025.

About 25 French centers are currently participating or in the process of activation.

The trial is registered under NCT05973864 :

https://www.clinicaltrials.gov/study/NCT05973864

Background

Triple-negative breast cancer (TNBC) represents approximately 15% of all breast cancers and is associated with a higher risk of early recurrence and poorer survival compared with other subtypes.

The addition of immunotherapy to neoadjuvant chemotherapy has significantly improved pathological complete response (pCR) rates and event-free survival (EFS) in early-stage TNBC, as demonstrated in pivotal trials such as KEYNOTE-522 ((Schmid *et al*., NEJM 2020; Schmid *et al.,* NEJM 2022; Schmid *et al.,* NEJM 2024).

However, patients who do **not achieve a pCR after neoadjuvant chemo-immunotherapy** remain at substantial risk of relapse, highlighting a persistent unmet clinical need in this population. Adjuvant pembrolizumab monotherapy is currently recommended, but the optimal strategy to further improve outcomes in patients with **residual invasive disease** is not yet established.

Capecitabine, an oral fluoropyrimidine, has previously demonstrated a significant survival benefit in TNBC patients with residual disease after neoadjuvant chemotherapy (not including immunotherapy) in the CREATE-X trial (Putzain *et al.*, Ann Oncol 2024).

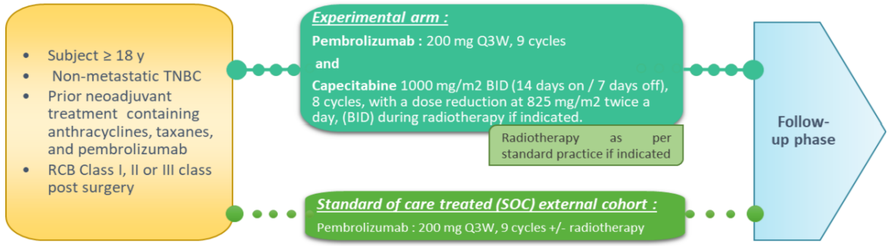
The CAPPA study therefore investigates whether **combining capecitabine with pembrolizumab** as adjuvant therapy can enhance efficacy without compromising safety, providing a rational and potentially synergistic approach to reducing recurrence risk in this high-risk TNBC subgroup.

Study design

CAPPA is a **multicenter, open-label, phase II study**.

Eligible patients are those with TNBC and residual disease after completion of neoadjuvant chemotherapy plus pembrolizumab.

- Experimental arm (N=220) : capecitabine (1250 mg/m², days 1–14, every 3 weeks × 8 cycles) + pembrolizumab (200 mg every 3 weeks × 9 cycles). Capecitabine is reduced at a dose of 825 mg/m2 BID during radiotherapy, performed as per standard practice, if indicated.
- Observational cohort (N=220) : real-world data from patients who received adjuvant pembrolizumab alone as standard of care or in previous studies.



Translational Research and ctDNA Blood Collection

Patients enrolled in the experimental arm undergo a predefined series of biological samplings for translational research.

- Archived FFPE (and frozen, if available) tumor samples from the pre-neoadjuvant biopsy and surgery are collected to determine TNBC histological subtype and explore biomarkers.
- Peripheral blood samples (**40 mL; 4 × 10 mL K_2-EDTA tubes**) are collected at the following timepoints: **Baseline (pre-treatment), Day 1 of Cycle 1, Day 1 of Cycle 2, End-of-treatment visit, Follow-up visits at 12 months and 24 months after inclusion.**

These samples are used for **ctDNA analyses** and for the identification of biomarkers associated with **immune-related adverse events** and treatment response.

Key inclusion/exclusion criteria

Inclusion Criteria

- Histologically confirmed triple-negative breast cancer (TNBC) defined as ER <10%, PR <10%, and HER2 negative (IHC 0–1+ or ISH non amplified).
- Residual invasive disease in breast and/or axillary lymph nodes after completion of neoadjuvant chemotherapy plus pembrolizumab.
- Completed adequate surgery with clear margins.
- ECOG performance status 0–1.
- Age ≥18 years and ability to comply with study procedures.
- Histologically confirmed TNBC, defined as HER2-negative (according to ASCO/CAP criteria) and <10% of cells staining positive for ER and PR by IHC;
- Patients who received standard neoadjuvant chemo-immunotherapy (minimum of 6 cycles);
- Absence of pCR, defined as RCB class I-III

Exclusion Criteria

- Evidence of metastatic disease or inflammatory breast cancer.
- Prior treatment with immune checkpoint inhibitors other than pembrolizumab.
- Concurrent malignancy or previous invasive cancer (except for adequately treated non-melanoma skin cancer or carcinoma in situ).
- Uncontrolled autoimmune disease or requirement for systemic corticosteroids/immunosuppressive therapy.
- Any condition that, in the investigator's opinion, could compromise patient safety or interfere with study participation.

Key study endpoints

Primary: To evaluate the efficacy of post-operative capecitabine added to pembrolizumab on **2-year invasive disease-free survival** (iDFS).

Secondary:

To assess the clinical impact of the capecitabine plus pembrolizumab combination in the target population in terms of:

- Distant disease-free survival (DDFS).
- Overall survival (OS).
- Efficacy (iDFS, OS and DDFS) of experimental arm will be compared to the external cohort
- Safety profile of the capecitabine plus pembrolizumab combination according to the use of radiation (yes/no) in the target population and

Exploratory translational analyses :

- Biomarker analyses on tumor tissue and blood samples.
- Imaging data for radiomic studies

References

- Schmid P, *et al*. Pembrolizumab for early triple-negative breast cancer. N Engl J Med. 2020.
- Schmid P, *et al*. Event-free survival with pembrolizumab in early TNBC. N Engl J Med. 2022.
- Schmid P, *et al*. Long-term outcomes with pembrolizumab in early TNBC. N Engl J Med. 2024.
- Putzain L, *et al*. Adjuvant treatment strategies for residual TNBC after neoadjuvant therapy. Ann Oncol. 2024.

This trial is funded by a French National Grant PHRC-K 2022.

This presentation is the intellectual property of the author/presenter. Contact them at cappa@unicancer.fr for permission to reprint and/or distribute.

Contact

Coordinator investigator :
Dr Delphine LOIRAT
Institut Curie and Institute of Women's cancers, Paris, France
Email: delphine.loirat@curie.fr

Sponsor:
Unicancer – UCBG
Paris, France
Email: cappa@unicancer.fr

© Poster Template by Genigraphics® 1.800.790.4001 www.genigraphics.com