OPT-PEMBRO: A Phase III Randomized Trial of Adjuvant Pembrolizumab Omission in Patients with Early-Stage Triple-Negative Breast Cancer Achieving Pathologic Complete Response After Neoadjuvant Chemo-Immunotherapy

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RATIONAL

- In early-stage triple-negative breast cancer (TNBC), the KEYNOTE-522 trial demonstrated that adding pembrolizumab to neoadjuvant chemotherapy, followed by continued adjuvant immunotherapy, significantly improved pathological complete response (pCR)[1], event-free survival[2], and overall survival[3], thereby establishing this regimen as the standard of care for stage II–III TNBC.
- Continuation of pembrolizumab post-surgery in all patients regardless of response raises concerns of overtreatment, toxicity, and cost.
- This is particularly evident in patients achieving pCR, who exhibit excellent long-term outcomes.

OPT-PEMBRO trial addresses whether adjuvant pembrolizumab can be safely omitted in patients achieving pCR after neoadjuvant chemo-immunotherapy

MAIN INCLUSION CRITERIA:

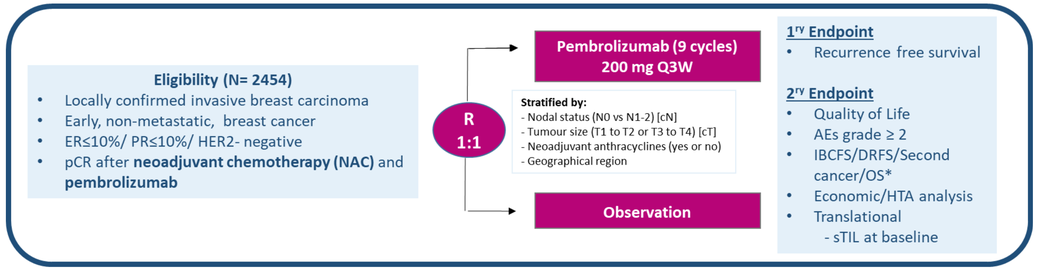
- Histologically documented **triple-negative/ER Low (ER≤10%) breast cancer**
- Stage **T1cN1-2 or T2-4N0-2** breast cancer according to AJCC 8th edition
- **Complete pathologic response** (pCR) after neoadjuvant chemotherapy and pembrolizumab
- Patients must have received adequate and complete resection of the primary tumor and adequate treatment of the axilla
- Patients must have received adequate locoregional radiation therapy
- Performance Status 0 or 1

MAIN EXCLUSION CRITERIA:

- History of invasive malignancy prior to the diagnosis of breast cancer without complete remission for more than 5 years, except for properly treated cervical carcinoma in situ and non-melanoma cancer of the skin
- Permanent pembrolizumab discontinuation during the neoadjuvant phase of treatment due to Pembrolizumab-related adverse events.
- Grade 3-4 pembrolizumab-related adverse events during the neoadjuvant phase of the treatment (except for endocrinopathies and dermatitis)
- Grade 1-2 pembrolizumab-related adverse events during the neoadjuvant phase of treatment that resolved but for which a dose >10 mg prednisone or equivalent is prescribed and ongoing.

DESIGN:

Pragmatic, multicentre, international, prospective, non-inferiority, two-arms, randomized (1:1), open-label, Phase III clinical study.



* IBCFS: Invasive Breast Cancer Free Survival; DRFS: Distant relapse free survival; OS: Overall survival

STUDY OBJECTIVES:

PRIMARY OBJECTIVE:

To determine the non-inferiority of Observation as compared to 6 months of adjuvant pembrolizumab after surgery in terms of **recurrence-free survival (RFS)** in patients who experienced pCR after neoadjuvant chemotherapy and pembrolizumab.

SECONDARY OBJECTIVES:

- Efficacy: invasive breast cancer-free survival (iBCFS), distant relapse-free survival (DRFS), second cancers and overall survival (OS)
- Quality of life: EORTC QLQ-C30, BR42, EQ-5D-5L
- Safety: Adverse events ≥ 2
- Immune-related adverse events (irAEs)
- Patient-reported outcomes (PRO-CTCAE)
- Fertility impact
- Economic evaluation
- Translational objective: TILs value at baseline and interaction with outcome.

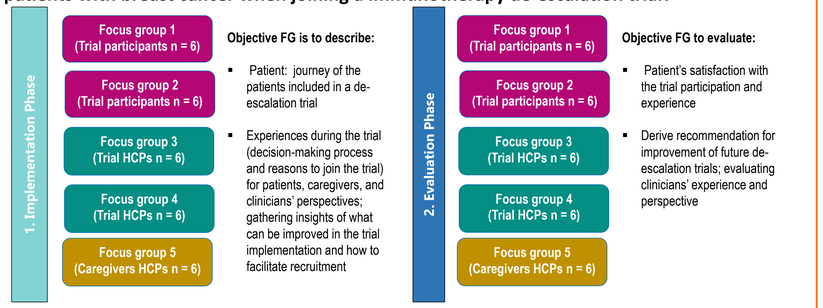
STATISTICAL ANALYSIS

- Non inferiority trial
- One-sided α = 0.025; Power = 85%
- Non-inferiority margin: HR = 1.44 (RFS 94% vs 91.5%)
- Planned sample size: 2,454 patients
- Follow-up: 10 years
- Interim analyses for futility are planned at 94 and 188 events.
- Analysis of the primary endpoint at 285 events.

Joint OptimICE-pCR & OPT-PEMBRO Prospective Meta-analysis

- A prospective meta-analysis with the U.S.-based OptimICE-pCR trial is agreed to maximize power, global relevance and strengthen external validity.
- Non inferiority margin to be considered unacceptable is 92% corresponding to a HR: 1,35
- 426 expected events provide 88% power at a one-sided α = 2.5% (HR = 1 under the alternative).

PATIENT INVOLVEMENT PLAN - What are the barriers, facilitators, and experiences of patients with breast cancer when joining a immunotherapy de-escalation trial?

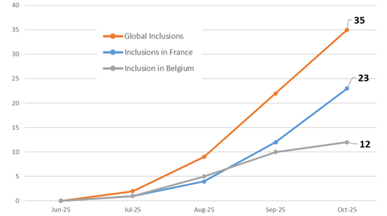


STUDY STATUS

As of October 30, 2025

- The first Initiation visit has been done in July 2025.
- The first patient was included on the 25th of July 2025; 2454 inclusions are expected with an inclusion period of 4 years.
- 2 Countries are activated :
  - ➢ 14 activated sites in France including 7 active sites
  - ➢ 9 activated sites in Belgium including 5 active sites
- 35 patients included

Enrolment curve



SIGNIFICANCE

- Together with OptimICE-pCR, **OPT-PEMBRO** aims to evaluate adjuvant pembrolizumab de-escalation in early TNBC.
- It addresses a key unanswered question from KEYNOTE-522 regarding the role of adjuvant immunotherapy in patients achieving pCR.
- By aiming to reduce toxicity, cost, and treatment burden without compromising survival,OPT-PEMBRO is expected to redefine post-neoadjuvant management in TNBC, establishing a new, evidence-based framework for immunotherapy duration.

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- Patients
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- Participating Sites

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