FR-POP: Real-World Data from 7,687 High-Risk TNBC Patients Treated with Perioperative Pembrolizumab in France

A. de Nonneville[1], D. Loirat[2], J. Ribeiro[3], S. Becourt[4], M.A. Benderra[5], N. Bénard[6], M. Campone[7], F. Dalenc[8], O. Derbel[9], I. Desmoulins[10], A. Deleuze[11], G. Emile[12], A. Gonçalves[1], J. Grenier[13], W. Jacot[14], C. Liautard[6], L. Mansi[15], M.A. Mouret Reynier[16], C. Perkins[6], B. Pistilli[3], J.P. Spano[17], A. Vasseur[18], F. Penault Llorca[16], and O. Tredan[19]

1 Aix-Marseille Univ, CNRS, INSERM, Institut Paoli-Calmettes, CRCM, Marseille, France. 2 Institut Curie- Institut of Women's Cancers, Paris, France. 3 Gustave Roussy, Villejuif, France. 4 Centre Oscar Lambret, Lille, France. 5 Department of Medical Oncology, Institut Universitaire de Cancérologie, Sorbonne University, AP-HP, Tenon Hospital, Paris, France. 6 Medical affairs, MSD, Puteaux, France. 7 Institut de Cancérologie de l'Ouest, Nantes, France. 8 Oncopole Claudius Regaud, Tuouse, France. 9 Hoptal privé Jean Mermoz, Lyon, France. 10 Centre Georges Francois Leclerc, Dijon, France. 11 Centre Eugene Marquis, Rennes, France. 12 François Baclesse Comprehensive Cancer Center, Caen, France. 13 Institut Sainte Catherine, Avignon, France. 14 Institut du Cancer de Montpellier, Montpellier University, INSERM U1194, Montpellier, France.15 CHRU Jean Minjoz, Besancon, France. 16 Centre Jean Perrin, Université Clermont Auvergne, INSERM, U1240 Imagerie Moléculaire et Stratégies Théranostiques, F-63000 Clermont Ferrand, France. 17 APHP, France. 18 Department of medical oncology, Institut Curie, Saint-Cloud, France. 19 Centre Léon Bérard, Lyon, France

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Introduction

- **KEYNOTE-522**[1] demonstrated that pembrolizumab added to neoadjuvant chemotherapy, followed by adjuvant administration, improved pathological complete response rate (pCR) and survival in early-stage triple-negative breast cancer (eTNBC), establishing a new standard of care.
- Based on these results, a **French Early Access Program** (EAP) was approved to provide pembrolizumab to patients before market authorization.
- This study aimed to describe **real-world survival outcomes** and **tolerance** of pembrolizumab in high-risk eTNBC patients treated through the French EAP.

Methods

Design
- Prospective national observational cohort via the French pembrolizumab EAP.
- Conducted from April 13, 2022, to November 20, 2024.

Eligibility
- Adults stage II–III eTNBC, including estrogen receptor-low (1–9%) per French guidelines.
- Not eligible for ongoing clinical trials.
- No hypersensitivity to pembrolizumab or its excipients.

Data collection
- Physician-completed EAP forms.
- Patient-reported EORTC QLQ-C30 questionnaires.

Follow-up
- Clinical and safety data recorded until treatment end or EAP closure.
- No post-treatment follow-up.

Results

Early access program overview

7,687 enrolled patients

1,259 physicians

427 healthcare centers

31 months

64% completion of the pembrolizumab initiation form; **2,454** patients with a surgery form

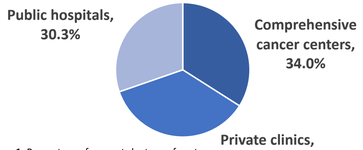


Figure 1. Percentage of requests by type of centers

Patient characteristics

Table 1: Characteristics of patients at treatment access request compared to KN-522 trial.

	FR-POP	KN-522 pembrolizumab group
Number of patients	7687	*784*
Women, % (n)	99.9 (7,683)	*99.9 (783)*
Age (years) median (range)	52.0 (19.0–92.0)	*49 (22.0–80.0)*
> 65 years, % (n)	21.8 (1,678)	*10.7 (84)*
Post-menopausal, % (n)	54.1 (3,993)	*44.0 (345)*
BMI (kg/m²), median (IQR)	25.2 (22.2 – 29.4)	*Not available*
Stage III, % (n)	39.1 (3,002)	*24.7 (194)*
ECOG PS ≥1, % (n)	14.3 (1,102)	*13.5 (106)*

Treatment overview

99.4% pembrolizumab 200 mg every 3 weeks

96.1% of chemo-pattern were carboplatin/ paclitaxel followed by anthracycline/ cyclophosphamide : Treatments matched the **KEYNOTE-522** regimen

188 median days from pembrolizumab request to surgery (around **6 months of neo-adjuvant treatment**)

29 days median interval between neoadjuvant completion and surgery

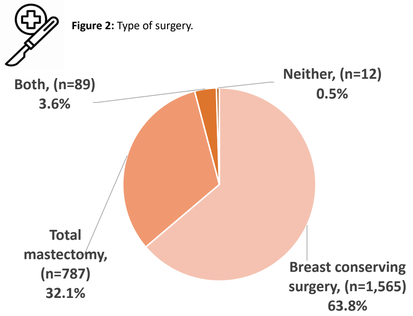


Figure 2: Type of surgery.

8.8% patients with **additional adjuvant systemic therapy**
- More frequent among patients with residual disease
- Most common: chemotherapy (54.2%, n=116), endocrine therapy (5.1%, n=11), olaparib (4.7%, n=10)

Of note, these off-label situations were reported to pharmacovigilance.

Pathological response

71.6% achieved pCR, **above the KEYNOTE-522 benchmark**

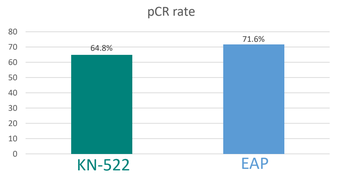


Figure 3: KEYNOTE-522 *versus* FR-POP pathological complete response.

- pCR rate was 64.8% for the patients who didn't receive the carboplatin/ paclitaxel followed by anthracycline/ cyclophosphamide chemo-pattern (3.71% of FR-POP).
- For patients who experienced treatment interruption due to immune toxicity (n=737), the pCR rate was 71.2% .
- The younger patients (<30y.o) had the higher pCR rate of 73.3% (n=45).

Quality-of-life

QLQ-C30 mean global health scores:
- **85.3** at neoadjuvant cycle 1 (n=423)
- **81.3** at adjuvant cycle 9 (n=40)

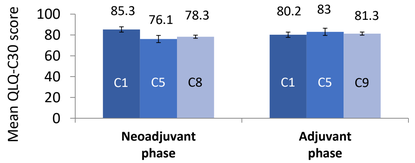


Figure 4: Quality-of-life scores (EORTC QLQ-C30).

Pembrolizumab interruptions

14.4% patients (n=1,105) with ≥1 pembrolizumab interruption

13 median days between first interruption and resumption

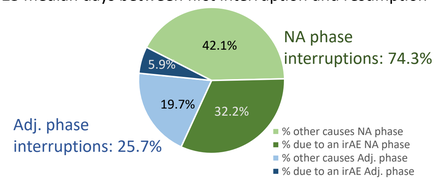
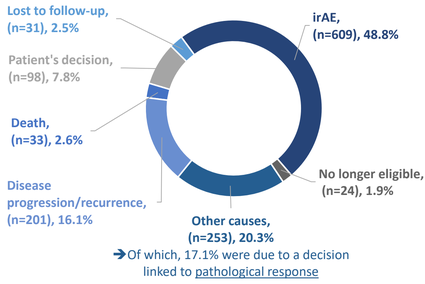


Figure 5: Pembrolizumab interruptions by treatment phase and proportions due to immune-related adverse events (irAE) and other causes.

Pembrolizumab discontinuations

16.1% patients (n=1,240) discontinued pembrolizumab



➔Of which, 17.1% were due to a decision linked to pathological response

Figure 6: Causes of reported pembrolizumab discontinuations, including the main 'other cause'.

Pharmacovigilance

Reported over the **31-months** period of the EAP:
- **417** serious treatment-related cases
- **8** deaths related to treatment

Key messages

- Real-world **pCR** of **71.6%** in a large real-life, non selected high-risk eTNBC population, consistent with **KEYNOTE-522** despite a high proportion of stage III and older patients.
- Pembrolizumab interruptions and discontinuations were mainly immune-related, underscoring the need for continued safety monitoring.

Limitations

- No follow-up for survival outcomes
- Incomplete safety data due to:
  - Potential underreporting of AEs in EAP.
  - No follow-up after treatment completion.
- Given the very low proportion of completed questionnaires, it is essential to emphasize the fragility of the QoL data.

Conclusions

- FR-POP represents one of the largest real-world cohorts of perioperative pembrolizumab in eTNBC.
- The **observed pCR rate above 70%** supports the external validity of **KEYNOTE-522** in routine practice, including among older patients.
- No delays in surgery was observed.
- Immune-related toxicity was the main cause of pembrolizumab interruptions and discontinuations. Eight treatment-related deaths demonstrate that continued vigilance is warranted. As experience increases and the IMMUNOTOX network is established in France, it is expected that severe toxicities will decrease.

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Contact

Chloé Perkins
MSD France
Email: chloe.perkins@msd.com
Phone: 0033630105253

Abbreviations

NA: Neoadjuvant
Adj.: Adjuvant
EAP: Early Access Program
eTNBC: Early stage triple negative breast cancer
EORTC QLQ-C30: EORTC Core Quality of Life questionnaire
ECOG-PS: Eastern Cooperative Oncology Group performance score
BMI: Body mass index
irAE: Immune-related adverse event
pCR: Pathological complete response
QoL : Quality of life

References

1. Schmid P, Cortes J, Pusztai L, *et al*. N Engl J Med. 2020;382(9):810-821. doi: 10.1056/NEJMoa1910549.