Clinical Updates From San Antonio

Triple-Negative Breast Cancer: Neoadjuvant/Adjuvant Immunotherapy

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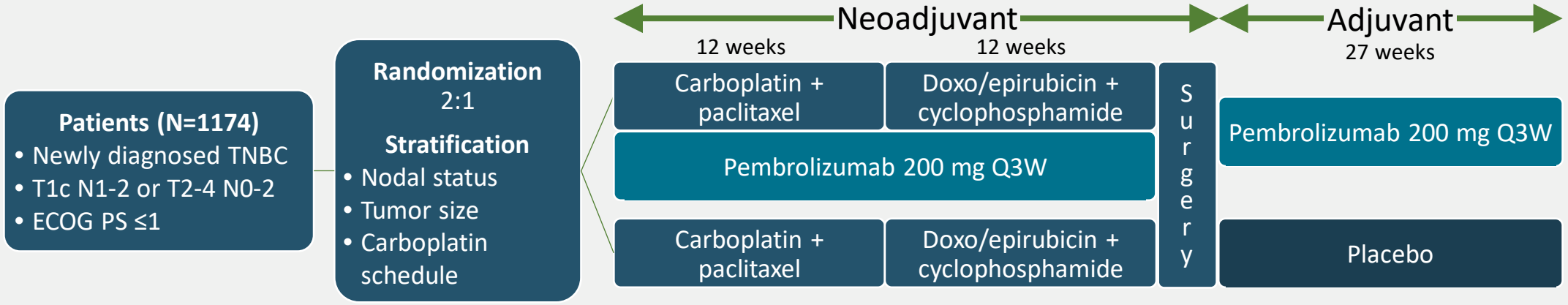
KEYNOTE-522 Trial Design



Primary Endpoints
- pCR at time of surgery
- EFS

Secondary Endpoints
- OS
- EFS (PD-L1+)
- pCR in all patients and patients with PD-L1+ tumors
- Safety

Exploratory Endpoint
- DPFS/DRFS

DPRS, distant progression-free survival; DRFS, distant recurrence-free survival; Doxo, doxorubicin; ECOG, Eastern Cooperative Group; EFS, event-free survival; N0, no regional LN metastases; N1-2, metastases to axillary lymph nodes or ipsilateral internal mammary nodes in the absence of axillary lymph node metastases; OS, overall survival; pCR, pathologic complete response; PD-L1, programmed death-ligand 1; PS, performance status; Q3W, every 3 weeks; T1c, tumor >1 cm but ≤2 cm; T2-4, tumor >2 cm but ≤5 cm, >5 cm, or any size with extension to the chest wall and/or skin; TNBC, triple-negative breast cancer.

Schmid P, et al. *N Engl J Med*. 2020;382(9):810-821; Schmid P, et al. *N Engl J Med*. 2022;386(6):556-567.

Comparison of Real-World and Phase 3 Efficacy and Safety of Treatment per KEYNOTE-522* in Patients With eTNBC†

Study	EHR Analysis (n=66)		KEYNOTE-522 (n=781)	
Population characteristics	T3/4: 48.1% N+: 53.2%		T3/4: 26% N+: 51.7%	
pCR rate, %	45.7 (n=55)		64.8 (N=784)	
AEs, %	Any grade	Grade ≥3	Any grade	Grade ≥3
Nausea	57.6	13.6	62.7	3.3
Neutropenia	78.7	62.1	46.7	34.6
Fatigue	71.2	27.3	41.1	3.5
Diarrhea	40.9	15.2	29.4	2.2
Peripheral neuropathy	39.4	9	19.7	1.9
Rash	12.1	4.5	21.8	0.9
imAEs, %	Any grade	Grade ≥3	Any grade	Grade ≥3
Hypothyroidism	18.2	4.5	13.7	0.4
Hyperthyroidism	1.5	1.5	4.6	0.3
Type 1 diabetes	3	3	0.3	0.3
Primary adrenal insufficiency	9	3	2.3	1.3
Colitis	9	7.6	1.7	0.9
Pancreatitis	3	1.5	0.5	0.5
Hepatitis	3	1.5	1.4	1.2
Pneumonitis	1.5	0	1.3	0.4
Ocular toxicity	3	1.5	0	0

*4 cycles of neoadjuvant pembrolizumab plus paclitaxel and carboplatin, followed by 4 cycles of pembrolizumab plus cyclophosphamide plus doxorubicin or epirubicin, and adjuvant pembrolizumab for up to 9 cycles; †Stage 2 or 3.

AE, adverse event; EHR, electronic health record; eTNBC, early triple-negative breast cancer; imAE; immune-mediated adverse event; N+, node positive; T3/4, tumor >5 cm/any size with extension to the chest wall and/or skin.

Hofherr M, et al. SABCS 2022. Abstract P3-06-06; Schmid P, et al. *N Engl J Med*. 2020;382(9):810-821; Schmid P, et al. *N Engl J Med*. 2022;386(6):556-567.

P3-06-06, Real-World Analysis of Adverse Events of Patients With Triple-Negative Breast Cancer Receiving Therapy per KEYNOTE-522

Patients Identified (N=79)

- Retrospective, single-center EHR analysis
- eTNBC with planned treatment per KN522*

Outcomes of Interest

- Treatment delays: number and length
- Treatment-related toxicities
- pCR rate

Hofherr M, Hedgecorth J, Ademuyiwa FO, Peterson LL, Bagegni NA, Suresh R, Frith A, Bose R, Weilbaecher K, Ma CX, Davis AA, Clifton KK

Study	EHR Analysis (N=79)
Population characteristics	T3/4: 48.1% N+: 53.7%
pCR rate, %	45.7 (n=55)
Hospitalizations ≥1	38
Emergency room visits ≥1	27
Treatment delays	40
Dose reductions	26

*4 cycles of neoadjuvant pembrolizumab plus paclitaxel and carboplatin, followed by 4 cycles of pembrolizumab plus cyclophosphamide plus doxorubicin or epirubicin, and adjuvant pembrolizumab for up to 9 cycles.

KN522, KEYNOTE-522.

Hofherr M, et al. SABCS 2022. Abstract P3-06-06.

P3-06-09, Real-World Toxicity of Pembrolizumab-Based Neoadjuvant Regimen in Patients With Early Triple-Negative Breast Cancer

Arnaud E, Alaoui K, Vaflard P, Korbi S, Meziani D, Thibault L, Desmaris R-P, Feron J-G, Pierga J-Y, Bidard F-C, Cottu P, Loirat D

Patients Identified (N=51)

- Ambispective, single-center analysis of clinical data
- eTNBC
- Treated per KN522*

Outcomes of Interest

- Efficacy
- Safety

Study	Ambispective cohort (N=51)	
Population characteristics	T3/4: 25% N+: 72.5%	
Median follow-up, months	5	
pCR rate, %	78.3 (KN522: 64.8)	
Postponement or discontinuation, %	34	
Dose reduction, %	19	
AEs (≥5%), %	Any grade	Grade ≥3
Any AE	100	76.5 (KN522: 76.8)
Anemia	100	37.3
Thrombocytopenia	37.3	11.8
Neutropenia	82.4	62.8
Febrile neutropenia	19.7	19.7
Peripheral neuropathy	47.1	2
imAEs (≥5%), %	49	17.6
Hypothyroidism	9.8	NA
Hyperthyroidism	7.8	3.9
Hypophysitis	5.9	NA
Troponine elevation	7.8	2

*4 cycles of neoadjuvant pembrolizumab plus paclitaxel and carboplatin, followed by 4 cycles of pembrolizumab plus cyclophosphamide plus doxorubicin or epirubicin, and adjuvant pembrolizumab for up to 9 cycles.

Arnaud E, et al. SABCS 2022. Abstract P3-06-09.

P3-06-10, Immune-Related Adverse Events (irAEs) and Pathological Complete Response (pCR) Rates in Patients Receiving Neoadjuvant Chemotherapy (CHT) and Pembrolizumab (PEM) for Early Triple-Negative Breast Cancer (eTNBC)

Marhold M, Udovica S, Wimmer K, Bago-Horvath Z, Robinson T, Fitzal F, Strasser-Weippl K, Bartsch R

Patients Identified (N=22)

- Prospective, multicenter analysis
- eTNBC
- Receiving treatment per KN522*

Outcomes of Interest

- imAE rate
- pCR rate

Study	Austrian (N=22)
Population characteristics	Mean T: 29mm (10-75) N+: 41%
pCR rate, %	50
Discontinuation before week 18, %	32
imAEs grade ≤2, %	50
Hypothyroidism	14
Arthritis	14
Hepatitis	5
Pneumonitis	5
imAEs grade ≥3, %	14
Myocarditis	9
Nephritis	5

*4 cycles of neoadjuvant pembrolizumab plus paclitaxel and carboplatin, followed by 4 cycles of pembrolizumab plus cyclophosphamide plus doxorubicin or epirubicin, and adjuvant pembrolizumab for up to 9 cycles.

Marhold M, et al. SABCS 2022. Abstract P3-06-10.