Pr KEYTRUDA®
(pembrolizumab)

KEYTRUDA® + CHEMOTHERAPY:
Helping patients fight locally recurrent unresectable or metastatic triple-negative breast cancer with PD-L1 expression CPS ≥ 10

KEYTRUDA® is indicated for adult patients in combination with chemotherapy with locally recurrent unresectable or metastatic triple-negative breast cancer (TNBC), who have not received prior chemotherapy for metastatic disease and whose tumors express PD-L1 (Combined Positive Score [CPS] ≥ 10) as determined by a validated test.

PD-L1=programmed death-ligand 1.

Evaluating KEYTRUDA® with chemotherapy in KEYNOTE-355*

Study endpoints

Major efficacy outcomes:

- Progression-free survival based on RECIST version 1.1 as assessed by BICR, modified to follow a maximum of 10 target lesions and a maximum of 5 target lesions per organ with tumor PD-L1 expression CPS ≥ 10
- Overall survival in patients with tumor PD-L1 expression CPS ≥ 10

Additional efficacy outcomes in patients with tumor PD-L1 expression CPS ≥ 10:

- Objective response rate
- Duration of response

All based on RECIST version 1.1 as assessed by BICR

KEYTRUDA® is indicated in adult patients in combination with chemotherapy with locally recurrent unresectable or metastatic triple-negative breast cancer (TNBC), who have not received prior chemotherapy for metastatic disease and whose tumors express PD-L1 (Combined Positive Score [CPS] ≥ 10) as determined by a validated test.

* Randomized, double-blind trial of KEYTRUDA® + chemotherapy vs. placebo + chemotherapy in treatment-naïve patients with locally recurrent inoperable or metastatic TNBC regardless of tumor PD L1 expression.# A total of 847 patients were randomized (2:1) and patients received either KEYTRUDA® 200 mg IV Q3W (n=556) or Placebo IV Q3W (n=281). Both arms were in combination with investigator's choice of chemotherapy: nab-paclitaxel 100 mg/m² on days 1, 8, and 15, every 28 days, paclitaxel 90 mg/m² on days 1, 8, and 15, every 28 days, gemcitabine 1000 mg/m² + carboplatin AUC 2 on days 1 and 8, every 21 days. Treatment with KEYTRUDA® or placebo continued until RECIST 1.1 defined progression of disease as determined by the investigator, unacceptable toxicity, or a maximum of 24 months. Administration of KEYTRUDA® was permitted beyond RECIST-defined disease progression if the patient was clinically stable and considered to be deriving clinical benefit by the investigator. Assessment of tumor status was performed at Weeks 8, 16, and 24, then every 9 weeks for the first year, and every 12 weeks thereafter.

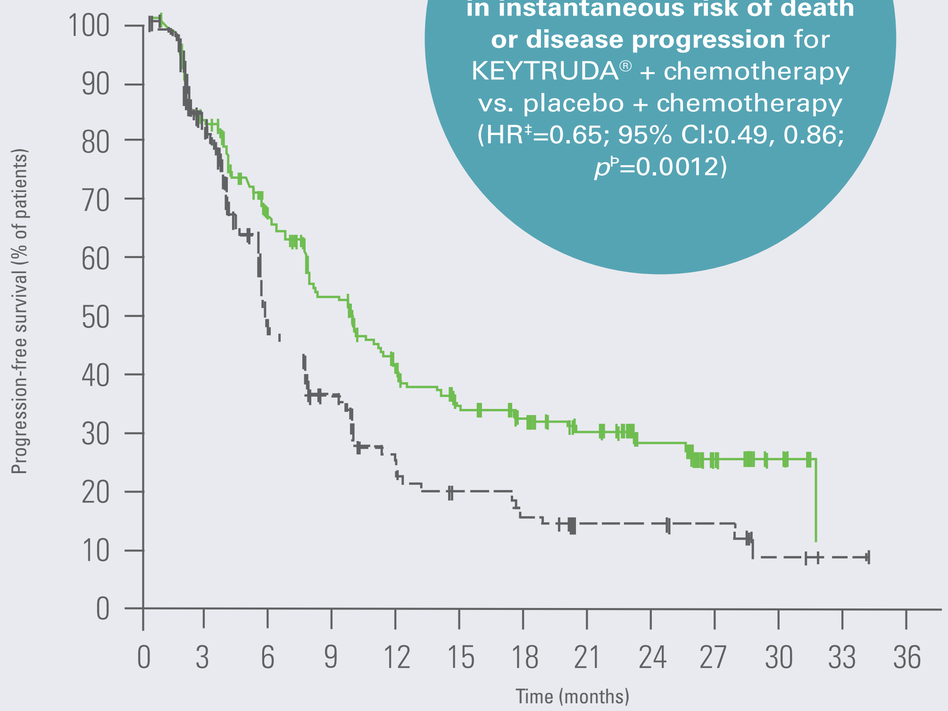
- NOTE: KEYTRUDA® is administered as an intravenous infusion over 30 minutes. The recommended dose of KEYTRUDA® in adults is either: 200 mg every 3 weeks or 400 mg every 6 weeks until disease progression, unacceptable toxicity or up to 24 months or 35 doses for 200 mg or 18 doses for 400 mg, whichever is longer, in patients without disease progression.

RECIST=Response Evaluation Criteria In Solid Tumors; IV=intravenous; Q3W=every 3 weeks; AUC=area under the curve; Q6W=every 6 weeks; BICR=Blinded Independent Central Review.

Efficacy results from the KEYNOTE-355 trial

KEYTRUDA® + chemotherapy demonstrated significant improvement in progression-free survival (PFS) vs. placebo + chemotherapy

Progression-free survival for KEYTRUDA® + chemotherapy vs. placebo + chemotherapy in patients with locally recurrent unresectable or metastatic TNBC with PD-L1 expression CPS ≥ 10



35% reduction
in instantaneous risk of death or disease progression for KEYTRUDA® + chemotherapy vs. placebo + chemotherapy (HR‡=0.65; 95% CI:0.49, 0.86; *p*Þ=0.0012)

Number at risk

KEYTRUDA® + chemotherapy	220	173	122	96	63	52	44	37	25	12	5	0
Placebo + chemotherapy	103	80	41	30	18	15	12	8	8	7		

Adapted from KEYTRUDA® Product Monograph.

Median Progression-Free Survival for patients with locally recurrent unresectable or metastatic TNBC with PD-L1 Expression CPS ≥ 10

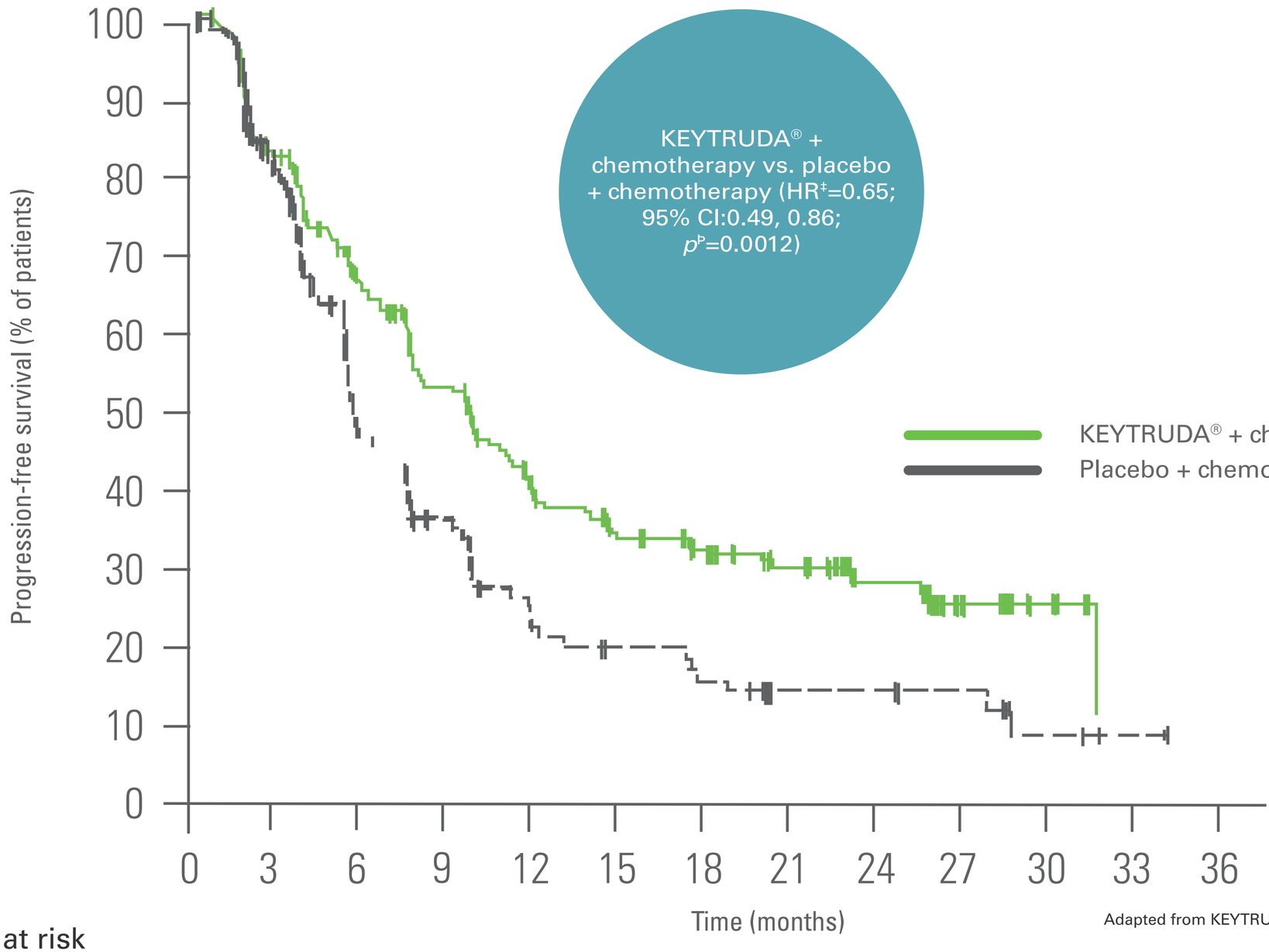
KEYTRUDA® + chemotherapy* (n=220)	**Placebo + chemotherapy*** (n=103)
9.7 months (95% CI: 7.6, 11.3)	**5.6 months** (95% CI: 5.3, 7.5)

* Chemotherapy: paclitaxel, nab-paclitaxel, or gemcitabine and carboplatin.

‡ Based on stratified Cox regression model.

§ One-sided p-Value based on stratified log-rank test (compared to a significance level of 0.0113).

Þ One-sided p-Value based on stratified log-rank test (compared to a significance level of 0.00411).



Adapted from KEYTRUDA® Product Monograph.

Number at risk

KEYTRUDA® + chemotherapy	220	173	122	96	63	52	44	37	25	12	5	0
Placebo + chemotherapy	103	80	41	30	18	15	12	8	8	7	3	1

Other efficacy results from the KEYNOTE-355 trial

Other efficacy outcomes in patients with PD-L1 expression CPS ≥ 10[†]

Objective response rate[†,‡]

KEYTRUDA® + chemotherapy* (n=220)	Placebo + chemotherapy* (n=103)
53% (95% CI: 46, 59)	**41%** (95% CI: 31, 51)

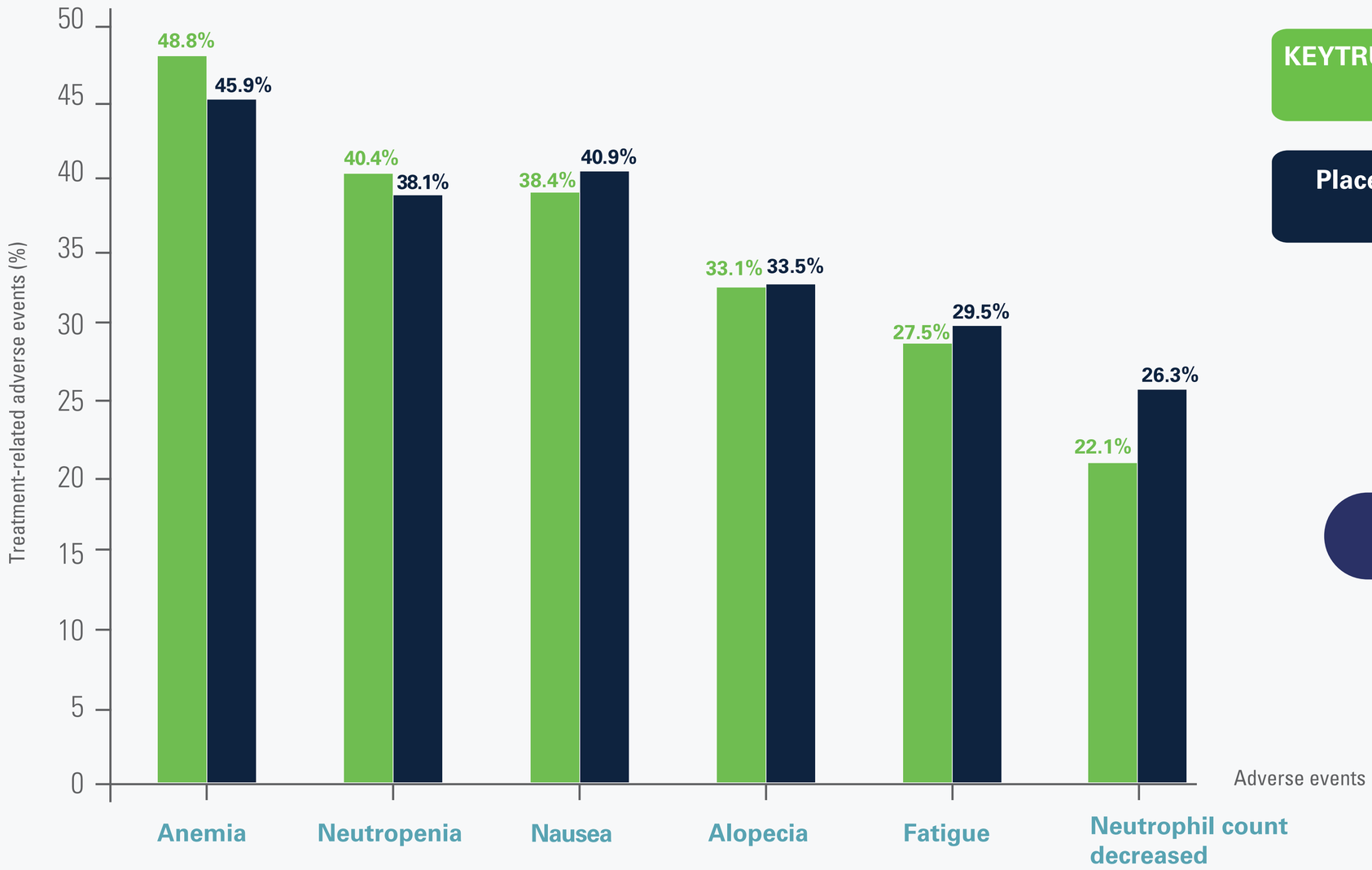
Duration of response, median in months (range)[†,§]

KEYTRUDA® + chemotherapy* (n=220)	Placebo + chemotherapy* (n=103)
12.8	**7.3**

* Chemotherapy: paclitaxel, nab-paclitaxel, or gemcitabine and carboplatin.
† Based on RECIST version 1.1 as assessed by BICR.
‡ Based on the pre-specified final analysis (data cutoff – 15 June 2021).
§ Based on a pre-specified interim analysis (data cutoff - 11 December 2019).
RECIST=Response Evaluation Criteria In Solid Tumors; BICR=Blinded Independent Central Review.

Demonstrated safety profile in locally recurrent unresectable or metastatic TNBC

Most common treatment-related adverse events (reported in ≥20% of patients) with either KEYTRUDA® + chemotherapy or placebo + chemotherapy, any grade in all patients as treated in KEYNOTE-355



More results >

More results

KEYTRUDA® was discontinued for treatment-related adverse events in **9.1% of patients**

Fatal treatment-related adverse events occurred in **0.3% of patients** receiving KEYTRUDA® in combination with chemotherapy including 1 case each of pneumonia and acute kidney injury

Serious treatment-related adverse events occurred in **17.6% of patients** receiving KEYTRUDA® in combination with chemotherapy

KEYTRUDA® was interrupted for treatment-related adverse events in **43% of patients**

Consider our data.
Choose KEYTRUDA® for eligible patients.

Recommended dosing regimen for locally recurrent unresectable or metastatic TNBC

Flexible dosing with KEYTRUDA®

KEYTRUDA® offers the flexibility of two dosing regimens:

Administered as an intravenous infusion over **30** minutes

Continue until:

- Disease progression
- Unacceptable toxicity
- Up to 24 months or 35 doses for 200 mg or 18 doses for 400 mg, whichever is longer, in patients without disease progression

When KEYTRUDA® is administered with chemotherapy, KEYTRUDA® should be administered first.

Refer to the Product Monographs for the chemotherapy agents administered in combination with KEYTRUDA® for recommended dosing information, as appropriate.

Missed dose

- Administer the missed dose as soon as possible.
- Adjust the schedule of administration to maintain the prescribed dosing interval.

TNBC=Triple-negative breast cancer; Q3W=once every 3 weeks; Q6W=once every 6 weeks.

KEYTRUDA® overview

KEYNOTE-355 summary

KEYTRUDA® was studied in combination with **3** chemotherapy options: nab-paclitaxel, paclitaxel, and gemcitabine + carboplatin in patients who had not been previously treated with chemotherapy and have locally recurrent unresectable or metastatic TNBC.

Progression-free survival
(RECIST version 1.1 as assessed by a BICR)

35% reduction in risk of instantaneous death or disease progression for KEYTRUDA® + chemotherapy vs. placebo + chemotherapy in patients with PD-L1 expression CPS ≥ 10 (HR=0.65; 95% CI: 0.49, 0.86; *p*=0.0012)

KEYTRUDA® + chemotherapy: 136/220 patients with event
vs. placebo + chemotherapy: 79/103 patients with event

Flexible dosing regimens

KEYTRUDA® offers 200 mg Q3W or 400 mg Q6W dosing.

Practice Guidelines

NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®*) for Breast Cancer[3]

Recurrent unresectable (local) or stage IV (M1) disease:

- Pembrolizumab + chemotherapy (albumin-bound paclitaxel, paclitaxel, or gemcitabine + carboplatin) is recommended as a preferred first-line therapy for PD-L1 CPS ≥ 10 triple-negative breast cancer.

Please see the NCCN Guidelines®* for detailed recommendations.

KEYTRUDA® + chemotherapy resulted in a significant improvement in progression-free survival compared with chemotherapy alone in patients with locally recurrent unresectable or metastatic TNBC patients with PD-L1 expression (CPS ≥10).

NCCN=National Comprehensive Cancer Network®* (NCCN®*).

Indications and clinical use:

KEYTRUDA® is indicated:

For treatment of adult patients with high-risk, early-stage, triple-negative breast cancer (TNBC) in combination with chemotherapy as neoadjuvant treatment, and then continued as monotherapy as adjuvant treatment after surgery.

For treatment of adult patients, in combination with chemotherapy, with locally recurrent unresectable or metastatic TNBC, who have not received prior chemotherapy for metastatic disease and whose tumours express PD-L1 (Combined Positive Score [CPS] ≥10) as determined by a validated test.

Pediatrics (<18 years of age): The safety and efficacy of KEYTRUDA® has not been established for pediatric patients.

Geriatrics (>65 years of age): No overall differences in safety or efficacy were reported between elderly patients (65 years and over) and younger patients (less than 65 years).

Relevant warnings and precautions:

- Immune-mediated adverse reactions, including severe and fatal cases:
  - Pneumonitis
  - Colitis
  - Hepatitis
  - Nephritis and renal dysfunction
  - Endocrinopathies including adrenal insufficiency, hypophysitis, type 1 diabetes mellitus and thyroid disorders
  - Severe skin reactions, including Stevens-Johnson syndrome and toxic epidermal necrolysis
- Other immune-mediated adverse events including uveitis, arthritis, myositis, encephalitis, sarcoidosis, myasthenic syndrome/myasthenia gravis, vasculitis, Guillain-Barré syndrome, hemolytic anemia, pancreatitis, myelitis, myocarditis, sclerosing cholangitis
- Solid organ transplant rejection
- Allogeneic stem cell transplant after and before treatment
- Severe infusion-related reactions
- Teratogenic risk
- Women should avoid pregnancy and breastfeeding during treatment and for at least 4 months after it
- Monitoring requirements
- Patients with hepatic impairment
- Renal impairment
- Driving and operating machinery
- Pediatrics
- Geriatrics

For more information:

Please consult the Product Monograph at https://www.merck.ca/confirm-monograph.xhtml?file=KEYTRUDA-PM_E.pdf for important information regarding adverse reactions, drug interactions, and dosing information which have not been discussed in this piece. The Product Monograph is also available by calling us at 1-800-567-2594 or by email at medinfocanada@merck.com.

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In locally recurrent unresectable or metastatic TNBC patients with PD-L1 expression (CPS ≥10) TNBC

CONSIDER KEYTRUDA®

References:

1. KEYTRUDA® Product Monograph. Merck Canada Inc. January 25, 2023. **2.** Cortes J, *et al*. Pembrolizumab plus chemotherapy versus placebo plus chemotherapy for previously untreated locally recurrent inoperable or metastatic triple-negative breast cancer (KEYNOTE-355): a randomized, placebo-controlled, double-blind, phase 3 clinical trial. *Lancet*. 2020;396(10265):1817-1828. **3.** Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines*) for Breast Cancer Version 3. 2022 — May 7, 2022. © National Comprehensive Cancer Network, Inc. 2021. All rights reserved. Accessed June 22, 2022. To view the most recent and complete version of the guideline, go online to NCCN.org. NCCN makes no warranties of any kind whatsoever regarding their content, use or application and disclaims any responsibility for their application or use in any way.

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