# Pembrolizumab (Keytruda®) in combination with chemotherapy as neo-adjuvant treatment, and then continued as monotherapy as adjuvant treatment after surgery, for the treatment of locally advanced, or early-stage triple-negative breast cancer (TNBC)

## General information

| Drug description | Indication [1] |
|---|---|
| Pembrolizumab (Keytruda®) is an anti–programmed death 1 (PD-1) monoclonal antibody. | Pembrolizumab (Keytruda®), in combination with chemotherapy as neo-adjuvant treatment, and then continued as monotherapy as adjuvant treatment after surgery, is indicated for the treatment of adults with locally advanced, or early-stage TNBC at high risk of recurrence. |

## Current treatment [2, 3]

- High-risk early TNBC is frequently associated with early recurrence and high mortality.
- Neo-adjuvant chemotherapy is the preferred treatment approach.
- Breast-conserving surgery (BCS) is the preferred local treatment option for the majority of early breast cancer patients, with the use of oncoplastic techniques, to maintain good cosmetic outcomes in technically challenging cases, when needed.
- Careful histological assessment of resection margins is essential. No tumour at the inked margin is required and >2 mm for in situ disease is preferred.
- Postoperative radiotherapy is strongly recommended after BCS.
- Boost radiotherapy is recommended to reduce the risk of in-breast relapse in patients at higher risk of local recurrence.
- Chemotherapy is recommended in the vast majority of triple-negative, HER2-positive breast cancers and in high-risk luminal-like HER2-negative tumours.
- Primary systemic therapy should be used to reduce the extent of surgery in locally advanced and large operable cancers, in particular when mastectomy is required due to tumour size. It should also be considered in all patients with tumours > 2 cm for which chemotherapy is deemed necessary, in particular with triple-negative and HER2-positive subtypes.
- The addition of a platinum compound may be considered in triple-negative tumours and/or in patients with deleterious BRCA1/2 mutations.
- In high-risk, triple-negative patients not achieving pathological complete response after standard neo-adjuvant chemotherapy, the addition of 6–8 cycles of capecitabine postoperatively may be considered.

## Regulatory status

### EMA [1, 4]

**Approval status for this indication**: On 22 April 2022, the CHMP adopted a positive opinion recommending a change to the terms of the marketing authorisation for Keytruda®.

The CHMP adopted a new indication as follows:

- Keytruda®, in combination with chemotherapy as neo-adjuvant treatment, and then continued as monotherapy as adjuvant treatment after surgery, is indicated for the treatment of adults with locally advanced, or early stage TNBC at high risk of recurrence.

**Other indications**: Keytruda® is indicated:

- **Melanoma**
  - as monotherapy for the treatment of adults and adolescents aged 12 years and older with advanced (unresectable or metastatic) melanoma.
  - as monotherapy for the adjuvant treatment of adults and adolescents aged 12 years and older with Stage IIB, IIC or III melanoma and who have undergone complete resection.
- **Non-small cell lung carcinoma (NSCLC)**
  - as monotherapy for the first-line treatment of metastatic NSCLC in adults whose tumours express PD-L1 with a ≥ 50% tumour proportion score (TPS) with no EGFR or ALK positive tumour mutations.
  - in combination with pemetrexed and platinum chemotherapy, for the first-line treatment of metastatic non-squamous NSCLC in adults whose tumours have no EGFR or ALK positive mutations.

### FDA [5, 6]

**Approval status for this indication**: On 26 July 2021, the FDA approved pembrolizumab (Keytruda®) for high-risk, early-stage, TNBC in combination with chemotherapy as neo-adjuvant treatment, and then continued as a single agent as adjuvant treatment after surgery.

- ✓ Priority review
- ✓ Breakthrough therapy designation

FDA also granted regular approval to pembrolizumab in combination with chemotherapy for patients with locally recurrent unresectable or metastatic TNBC whose tumours express PD-L1 (CPS ≥10) as determined by an FDA approved test. FDA granted accelerated approval to pembrolizumab for this indication in November 2020.

**Other indications**: Keytruda® is indicated:

- **Melanoma**
  - for the treatment of patients with unresectable or metastatic melanoma.
  - for the adjuvant treatment of adult and paediatric (12 years and older) patients with Stage IIB, IIC, or III melanoma following complete resection.
- **NSCLC**
  - in combination with pemetrexed and platinum chemotherapy, as first-line treatment of patients with metastatic non-squamous NSCLC, with no EGFR or ALK genomic tumour aberrations.
  - in combination with carboplatin and either paclitaxel or paclitaxel protein-bound, as first-line treatment of patients with metastatic squamous NSCLC.

- in combination with carboplatin and either paclitaxel or nab-paclitaxel, for the first-line treatment of metastatic squamous NSCLC in adults.
- as monotherapy for the treatment of locally advanced or metastatic NSCLC in adults whose tumours express PD-L1 with a ≥ 1% TPS and who have received at least one prior chemotherapy regimen. Patients with EGFR or ALK positive tumour mutations should also have received targeted therapy before receiving Keytruda®.

❖ **Classical Hodgkin lymphoma (cHL)**
- as monotherapy for the treatment of adult and paediatric patients aged 3 years and older with relapsed or refractory cHLwho have failed autologous stem cell transplant (ASCT) or following at least two prior therapies when ASCT is not a treatment option.

❖ **Urothelial carcinoma**
- as monotherapy for the treatment of locally advanced or metastatic urothelial carcinoma in adults who have received prior platinum-containing chemotherapy.
- as monotherapy for the treatment of locally advanced or metastatic urothelial carcinoma in adults who are not eligible for cisplatin-containing chemotherapy and whose tumours express PD-L1 with a combined positive score (CPS) ≥ 10.

❖ **Head and neck squamous cell carcinoma (HNSCC)**
- as monotherapy or in combination with platinum and 5-fluorouracil (5-FU) chemotherapy, for the first-line treatment of metastatic or unresectable recurrent HNSCC in adults whose tumours express PD-L1 with a CPS ≥ 1.
- as monotherapy for the treatment of recurrent or metastatic HNSCC in adults whose tumours express PD-L1 with a ≥ 50% TPS and progressing on or after platinum-containing chemotherapy.

❖ **Renal cell carcinoma (RCC)**
- in combination with axitinib, for the first-line treatment of advanced RCC in adults.
- in combination with lenvatinib, for the first-line treatment of advanced RCC in adults.
- as monotherapy for the adjuvant treatment of adults with RCC at increased risk of recurrence following nephrectomy, or following nephrectomy and resection of metastatic lesions.

❖ **Microsatellite instability high (MSI-H) or mismatch repair deficient (dMMR) cancers**
- **Colorectal cancer (CRC)**
  - as monotherapy for adults with MSI-H or dMMR CRC in the following settings:
    - first-line treatment of metastatic CRC;
    - treatment of unresectable or metastatic CRC after previous fluoropyrimidine-based combination therapy.
- **Non-colorectal cancers**
  - as a single agent for the first-line treatment of patients with NSCLC expressing PD-L1 (TPS≥1%) as determined by an FDA-approved test, with no EGFR or ALK genomic tumor aberrations, and is:
    - stage III where patients are not candidates for surgical resection or definitive chemoradiation, or
    - metastatic.
  - as a single agent for the treatment of patients with metastatic NSCLC whose tumors express PD-L1 (TPS ≥1%) as determined by an FDA-approved test, with disease progression on or after platinum-containing chemotherapy. Patients with EGFR or ALK genomic tumor aberrations should have disease progression on FDA-approved therapy for these aberrations prior to receiving Keytruda®.

❖ **HNSCC**
- in combination with platinum and FU for the first-line treatment of patients with metastatic or with unresectable, recurrent HNSCC.
- as a single agent for the first-line treatment of patients with metastatic or with unresectable, recurrent HNSCC whose tumours express PD-L1 (CPS ≥1) as determined by an FDA-approved test.
- as a single agent for the treatment of patients with recurrent or metastatic HNSCC with disease progression on or after platinum-containing chemotherapy.

❖ **cHL**
- for the treatment of adult patients with relapsed or refractory cHL.
- for the treatment of paediatric patients with refractory cHL, or cHL that has relapsed after 2 or more lines of therapy.

❖ **Primary mediastinal large B-cell lymphoma (PMBCL)**
- for the treatment of adult and paediatric patients with refractory PMBCL, or who have relapsed after 2 or more prior lines of therapy. **Limitations of Use**: Keytruda® is not recommended for treatment of patients with PMBCL who require urgent cytoreductive therapy.

❖ **Urothelial carcinoma**
- for the treatment of patients with locally advanced or metastatic urothelial carcinoma who:
  - are not eligible for any platinum-containing chemotherapy, or
  - who have disease progression during or following platinum-containing chemotherapy or within 12 months of neo-adjuvant or adjuvant treatment with platinum-containing chemotherapy.
- for the treatment of patients with Bacillus Calmette-Guerin-unresponsive, high-risk, non-muscle invasive bladder cancer with carcinoma in situ with or without papillary tumours who are ineligible for or have elected not to undergo cystectomy.

❖ **MSI-H or dMMR cancer**
- for the treatment of adult and paediatric patients with unresectable or metastatic, MSI-H or dMMR solid tumours that have progressed following prior treatment and who have no satisfactory alternative treatment options (indication approved under accelerated approval based on tumour response rate and durability of response). **Limitations of Use**: The safety and effectiveness of Keytruda® in paediatric patients with MSI-H central nervous system cancers have not been established.

❖ **MSI-H or dMMR CRC**

- as monotherapy for the treatment of the following MSI-H or dMMR tumours in adults with:
  - advanced or recurrent endometrial carcinoma (EC), who have disease progression on or following prior treatment with a platinum-containing therapy in any setting and who are not candidates for curative surgery or radiation;
  - unresectable or metastatic gastric, small intestine, or biliary cancer, who have disease progression on or following at least one prior therapy.

❖ **Oesophageal carcinoma**
- in combination with platinum and fluoropyrimidine-based chemotherapy, for the first-line treatment of locally advanced unresectable or metastatic carcinoma of the oesophagus or HER-2 negative gastroesophageal junction adenocarcinoma, in adults whose tumours express PD-L1 with a CPS ≥ 10.

❖ **TNBC**
- in combination with chemotherapy, for the treatment of locally recurrent unresectable or metastatic TNBC in adults whose tumours express PD-L1 with a CPS ≥ 10 and who have not received prior chemotherapy for metastatic disease.

❖ **EC**
- in combination with lenvatinib, for the treatment of advanced or recurrent EC in adults who have disease progression on or following prior treatment with a platinum-containing therapy in any setting and who are not candidates for curative surgery or radiation.

❖ **Cervical cancer**
- in combination with chemotherapy with or without bevacizumab, for the treatment of persistent, recurrent, or metastatic cervical cancer in adults whose tumours express PD-L1 with a CPS ≥ 1.

✓ **Medicine under additional monitoring**

- for the treatment of patients with unresectable or metastatic MSI-H or dMMR CRC.

❖ **Gastric cancer**
- in combination with trastuzumab, fluoropyrimidine- and platinum-containing chemotherapy, for the first-line treatment of patients with locally advanced unresectable or metastatic HER2-positive gastric or gastroesophageal junction (GEJ) adenocarcinoma (indication approved under accelerated approval based on tumour response rate and durability of response).

❖ **Oesophageal cancer**
- for the treatment of patients with locally advanced or metastatic oesophageal or GEJ (tumours with epicenter 1 to 5 centimeters above the GEJ) carcinoma that is not amenable to surgical resection or definitive chemoradiation either:
  - in combination with platinum- and fluoropyrimidine-based chemotherapy, or
  - as a single agent after one or more prior lines of systemic therapy for patients with tumours of squamous cell histology that express PD-L1 (CPS ≥10) as determined by an FDA-approved test.

❖ **Cervical cancer**
- in combination with chemotherapy, with or without bevacizumab, for the treatment of patients with persistent, recurrent, or metastatic cervical cancer whose tumours express PD-L1 (CPS ≥1) as determined by an FDA-approved test.
- as a single agent for the treatment of patients with recurrent or metastatic cervical cancer with disease progression on or after chemotherapy whose tumours express PD-L1 (CPS ≥1) as determined by an FDA-approved test.

❖ **Hepatocellular carcinoma (HCC)**
- for the treatment of patients with HCC who have been previously treated with sorafenib (indication approved under accelerated approval based on tumour response rate and durability of response).

❖ **Merkel cell carcinoma (MCC)**
- for the treatment of adult and paediatric patients with recurrent locally advanced or metastatic MCC (indication approved under accelerated approval based on tumour response rate and durability of response).

❖ **RCC**
- in combination with axitinib, for the first-line treatment of adult patients with advanced RCC.
- in combination with lenvatinib, for the first-line treatment of adult patients with advanced RCC.
- for the adjuvant treatment of patients with RCC at intermediate-high or high risk of recurrence following nephrectomy, or following nephrectomy and resection of metastatic lesions.

❖ **EC**
- in combination with lenvatinib, for the treatment of patients with advanced EC that is not MSI-H or dMMR, who have disease progression following prior systemic therapy in any setting and are not candidates for curative surgery or radiation.
- as a single agent, for the treatment of patients with advanced EC that is MSI-H or dMMR, as determined by an FDA-approved test, who have disease progression following prior systemic therapy in any setting and are not candidates for curative surgery or radiation.

❖ **Tumour mutational burden-high (TMB-H) cancer**
- for the treatment of adult and paediatric patients with unresectable or metastatic TMB-H (≥10 mutations/megabase) solid tumours, as determined by an FDA-approved test, that have

progressed following prior treatment and who have no satisfactory alternative treatment options (indication approved under accelerated approval based on tumour response rate and durability of response). **Limitations of Use**: The safety and effectiveness of Keytruda® in paediatric patients with TMB-H central nervous system cancers have not been established.

- ❖ **Cutaneous squamous cell carcinoma (cSCC)**
  - for the treatment of patients with recurrent or metastatic cSCC or locally advanced cSCC that is not curable by surgery or radiation.
- ❖ **TNBC**
  - in combination with chemotherapy, for the treatment of patients with locally recurrent unresectable or metastatic TNBC whose tumours express PD-L1 (CPS ≥10) as determined by an FDA approved test.
- ❖ **Adult indications: Additional dosing regimen of 400 mg every 6 weeks**
  - for use at an additional recommended dosage of 400 mg every 6 weeks for all approved adult indications (indication is approved under accelerated approval based on pharmacokinetic data, the relationship of exposure to efficacy, and the relationship of exposure to safety).

## Costs

4 ml Keytruda® concentrate for solution for infusion 25mg/ml = **€3,428.00** (ex-factory price) [7].

## Warnings and precautions [6]

- ❖ **Immune-mediated adverse reactions**
  - Immune-mediated adverse reactions, which may be severe or fatal, can occur in any organ system or tissue, including the following: immune-mediated pneumonitis, immune-mediated colitis, immune-mediated hepatitis, immune-mediated endocrinopathies, immune-mediated nephritis with renal dysfunction, immune-mediated dermatologic adverse reactions, and solid organ transplant rejection.
  - Monitor for early identification and management. Evaluate liver enzymes, creatinine, and thyroid function at baseline and periodically during treatment.
  - Withhold or permanently discontinue based on severity and type of reaction.
- ❖ **Infusion-related reactions**
  - Interrupt, slow the rate of infusion, or permanently discontinue Keytruda® based on the severity of reaction.
- ❖ **Complications of allogeneic HSCT**
  - Fatal and other serious complications can occur in patients who receive allogeneic HSCT before or after being treated with a PD-1/PD-L1 blocking antibody.
- ❖ Treatment of patients with **multiple myeloma** with a PD-1 or PD-L1 blocking antibody in combination with a thalidomide analogue plus dexamethasone is not recommended outside of controlled clinical trials.
- ❖ **Embryo-foetal toxicity**
  - Can cause foetal harm. Advise females of reproductive potential of the potential risk to a foetus and to use effective method of contraception.

## Study characteristics [3, 8-10]

| Trial name | n | Intervention (I) | Comparator (C) | PE | Characteristics | Biomarker | Funding | Publication(s) |
|---|---|---|---|---|---|---|---|---|
| KEYNOTE-522 NCT03036488 | 1174 2:1 | Neo-adjuvant therapy with 4 cycles of **pembrolizumab** (at a dose of 200 mg) every 3 weeks **+** | **placebo** every 3 weeks **+** paclitaxel and carboplatin **followed by** an additional 4 | **pathological complete response**[2] at the time of definitive surgery and **event-free** | **ongoing**[3], randomised, double-blind phase 3 trial | PD-L1 | Merck Sharp & Dohme | [3] |

[2] Defined as pathological stage ypTo/Tis ypNo.
[3] The KEYNOTE-522 trial is currently ongoing; estimated study completion date is 09/2025.

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | | paclitaxel and carboplatin **followed by** an additional 4 cycles of pembrolizumab or placebo **+** doxorubicin–cyclophosphamide or epirubicin–cyclophosphamide[1] | cycles of pembrolizumab or placebo **+** doxorubicin–cyclophosphamide or epirubicin–cyclophosphamide | **survival** in the ITT-population | | | | |

| **Efficacy** (I vs. C), interim analysis data | **Safety** (I vs. C), interim analysis data |
|---|---|
| **Primary analysis (data cutoff, 24 September 2018) among the first 602 patients who underwent randomisation**<br>**Complete response** (pathological stage ypTo/Tis ypNo): 64.8% vs. 51.2%; estimated treatment difference, 13.6 percentage points (95% CI 5.4-21.8; p<0.001)<br>**Pathological complete response (stage ypTo/Tis ypNo) in the PD-L1–positive population**: 68.9% vs. 54.9%<br>**Pathological complete response (stage ypTo/Tis ypNo) in the PD-L1–negative population**: 45.3% vs. 30.3%<br>**Kaplan–Meier estimates of the percentage of patients at 18 months** who were alive without disease progression that precluded definitive surgery, without local or distant recurrence, and without a second primary tumour: 91.3% (95% CI 88.8-93.3) vs. 85.3% (95% CI 80.3-89.1); **median**: NR in either group<br>**HR for disease progression** (precluding definitive surgery), local or distant recurrence or a second primary tumour, or death from any cause favoured the pembrolizumab–chemotherapy group (HR, 0.63; 95% CI 0.43-0.93).<br><br>**UPDATE from a pre-specified interim analysis, median follow-up time for all patients was 37.8 months (range: 2.7-48 months) [4]:**<br>Pathological complete response rate (ypTo/Tis ypNo): 64.0% vs. 54.7%; p=0.00221<br>24 month event-free survival rate: 87.8% vs. 81.0%; HR 0.63 (95% CI, 0.48-0.82); p=0.00031<br>24-month OS rate: 92.3% vs. 91.0%; HR 0.72 (0.51-1.02)<br><br>**UPDATE from the fourth planned interim analysis (median follow up 39.1 months) [11]:**<br>HR for event or death: 0.63 (95% CI, 0.48-0.82; p<0.001)<br>Estimated event-free survival at 36 months: 84.5% (95% CI, 81.7 to 86.9) vs. 76.8% (95% CI, 72.2-80.7)<br>Median event-free survival: not reached in either group<br>HR for distant progression, distant recurrence, or death: 0.61 (95% CI, 0.46-0.82)<br>Data on overall survival: immature at the time of analysis<br>Patients who died: 10.2% and 14.1%; HR 0.72 (95 CI, 0.51-1.02)<br>Estimated OS at 36 months: 89.7% (95% CI, 87.3-91.7) vs. 86.9% (95% CI, 83.0-89.9) | **Neo-adjuvant phase**<br>**AEs of any grade that were considered by the investigators to be related to the trial treatment:** 99.0% vs. 99.7%<br>**Treatment-related AEs ≥grade 3:** 76.8% vs. 72.2%<br>**Serious treatment-related AEs:** 32.5% vs. 19.5%<br>**Treatment-related AEs led to discontinuation of any trial drug:** 23.3% vs. 12.3%<br><br>**Adjuvant phase**<br>**Treatment-related AEs:** 48.1% vs. 43.0%<br><br>**Across both phases**<br>**Treatment-related AEs led to death:** 3 (0.4%)[4] vs. and 1 (0.3%)[5]<br><br>**UPDATE from the fourth planned interim analysis (median follow up 39.1 months) [11]:**<br>AEs of grade ≥3 that were considered by the investigator to be related to trial treatment: 77.1% vs. 73.3%<br>Discontinuation of the trial regimen due to treatment-related AEs: 27.7% vs. 14.1%<br>Serious treatment-related AEs: 34.1% vs. 20.1%<br>Treatment-related AEs leading to death: 0.5% vs. 0.3%<br>Immune-mediated AEs of any grade: 33.5% vs. 11.3% |

[1] Patients were randomly assigned, in a 2:1 ratio, to receive either pembrolizumab or placebo. In the neo-adjuvant phase, they received 4 cycles of an IV infusion of pembrolizumab (200 mg) or placebo once every 3 weeks plus paclitaxel (80 mg/m² of BSA once weekly) plus carboplatin (at a dose based on an area under the concentration–time curve of 5 mg per ml/min once every 3 weeks or 1.5 mg per ml/min once weekly in the first 12 weeks) (first neo-adjuvant treatment), followed by 4 cycles of pembrolizumab or placebo plus doxorubicin (60 mg/m²) or epirubicin (90 mg/m²) plus cyclophosphamide (600 mg/m² once every 3 weeks in the subsequent 12 weeks) (second neo-adjuvant treatment).

[4] 1 from pulmonary embolism, 1 from sepsis and multiple organ dysfunction syndrome, and 1 from pneumonitis.

[5] Due to septic shock.

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|---|---|
| Median OS: not reached in either group<br>The prespecified, non-randomised, exploratory analysis of event-free survival conducted according to the outcome (yes or no) of pathological complete response (ypTo–Tis ypNo) showed that patients who had an event or died (among patients with a pathological complete response): 5.5% vs. 7.4%, HR 0.73; 95% CI, 0.39-1.36<br>Patients who had an event or died (among patients without a pathological complete response): 33.1% vs. 44.5%; HR 0.70; 95% CI, 0.52-0.95) | Immune-mediated AEs of grade ≥3: 12.9% vs. 1.0%<br>Immune-mediated adverse events leading to death: 0.3% vs. 0 |

**ESMO-MCBS version 1.1 [12]**

| Scale | Int. | Form | MG ST | MG | HR (95% CI) | Score calculation | PM | Toxicity | QoL | AJ | FM |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Original | adjuvant | 1 | - | 24-months DFS: +6,8% | 0.63 (0.48-0.82) | Improvements in DFS alone (HR<0.65) in studies without mature survival data | A | - | - | - | A |
| Adapted | adjuvant | 1 | - | 24-months DFS: +6,8% | 0.63 (0.48-0.82) | Improvements in DFS alone (HR<0.65) in studies without mature survival data | A | - | - | - | A |

**Risk of bias (RCT) [13]**

| Adequate generation of randomisation sequence | Adequate allocation concealment | Blinding | Selective outcome reporting unlikely | Other aspects which increase the risk of bias | **Risk of bias** |
|---|---|---|---|---|---|
| yes | yes | yes | unclear[6] | yes[7] | unclear |

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**Last updated**: 09/2022

Abbreviations: AE=adverse event, AJ=adjustment, ALK=anaplastic lymphoma kinase, ASCT=autologous stem cell transplant, BCS=breast-conserving surgery C=comparator, cHL=classical Hodgkin lymphoma, CHMP=Committee for Medicinal Products for Human Use, CI=confidence interval, CPS=combined positive score, CRC=colorectal cancer, cSCC=cutaneous squamous cell carcinoma, DFS=disease-free survival, dMMR=mismatch repair deficient, EC=endometrial cancer, EGFR=epidermal growth factor receptor, EMA=European Medicines Agency, ESMO-MCBS= European Society of Medical Oncology – Magnitude of Clinical Benefit Scale, FDA=Food and Drug Administration, FM=final magnitude of clinical benefit grade, GEJ=gastroesophageal junction, HCC=hepatocellular carcinoma, HER2=human epidermal growth factor receptor 2, HNSCC=head and neck squamous cell carcinoma, HR=hazard ratio, HSCT=haematopoietic stem cell transplantation, I=intervention, Int.=intention, ITT=intention-to-treat, MCC=Merkel cell carcinoma, MG=median gain, MSI-H=microsatellite instability-high, n=number of patients, NSCLC=non-small cell lung carcinoma, OS=overall survival, PD-1= anti–programmed death 1, PD-L1=programmed ligand-1, PE=primary endpoint, PFS=progression-free survival, PM=preliminary grade, PMBCL=primary mediastinal large B-cell lymphoma, QoL=quality of life, RCC=renal cell carcinoma, SAE=serious adverse event, ST=standard treatment, TMB-H=tumour mutational burden-high, TNBC=triple-negative breast cancer, TPS=tumour proportion score

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[6] The KEYNOTE-533 trial is ongoing; hence, currently only interim analysis results are available.
[7] The trial was developed by a scientific advisory committee and employees of the sponsor. The first draft of the manuscript was written by the first author with editorial assistance provided by a medical writer employed by the sponsor.

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