TECENTRIQ®

Atezolizumab

Information as set forth in this label only applies to Tecentriq

1. DESCRIPTION

1.1 THERAPEUTIC/PHARMACOLOGIC CLASS OF DRUG

Antineoplastic agent, humanized immunoglobulin G1 (IgG1) monoclonal antibody.

ATC Code – L01FF05.

1.2 TYPE OF DOSAGE FORM

Concentrate for solution for infusion.

1.3 ROUTE OF ADMINISTRATION

Intravenous (IV) Infusion.

1.4 STERILE/RADIOACTIVE STATEMENT

Sterile product.

1.5 QUALITATIVE AND QUANTITATIVE COMPOSITION

Active ingredient: atezolizumab

Tecentriq is supplied as a single-use vials containing preservative-free, colorless to slightly yellow solution, at an active ingredient concentration of 60 mg/mL as follows:

- 14 mL vial containing a total of 840 mg atezolizumab
- 20 mL vial containing a total of 1200 mg atezolizumab

Excipients: L-histidine, glacial acetic acid, sucrose, polysorbate 20, water for injection.

2. CLINICAL PARTICULARS

2.1 THERAPEUTIC INDICATION(S)

Urothelial Carcinoma (second-line)

Tecentriq is indicated for the treatment of patients with locally advanced or metastatic urothelial carcinoma (UC) after prior platinum-containing chemotherapy.

Early-Stage Non-Small Cell Lung Cancer

Tecentriq as monotherapy is indicated as adjuvant treatment following resection and platinum-based chemotherapy for patients with stage II to IIIA (7th edition of the UICC/AJCC-staging system) NSCLC whose tumors have PD-L1 expression on ≥ 1% of tumor cells (TC).

DISETUJUI OLEH BPOM 8 MEI 2025 ID REG: EREG10043712400408-09

Metastatic Non-Small Cell Lung Cancer

Tecentriq is indicated for the treatment of patients with locally advanced or metastatic non-small cell lung cancer (NSCLC) after prior platinum-containing chemotherapy.

Tecentriq as monotherapy is indicated for the first-line treatment of patients with metastatic NSCLC whose tumors have a PD-L1 expression ≥ 50% tumor cells or ≥ 10% tumor-infiltrating immune cells and who do not have EGFR or ALK genomic tumor aberrations.

Tecentriq, in combination with bevacizumab, paclitaxel, and carboplatin, is indicated for the first-line treatment of adult patients with metastatic non-squamous NSCLC with no EGFR or ALK genomic tumor aberrations.

Small Cell Lung Cancer

Tecentriq, in combination with carboplatin and etoposide, is indicated for the first-line treatment of patients with extensive-stage small cell lung cancer (ES-SCLC).

Hepatocellular Carcinoma

Tecentriq, in combination with bevacizumab (Avastin), is indicated for the treatment of patients with unresectable hepatocellular carcinoma (HCC) who have not received prior systemic therapy.

2.2 DOSAGE AND ADMINISTRATION

General

Tecentriq must be administered as an intravenous infusion under the supervision of a qualified health care professional. Do not administer as an IV push or bolus.

Do not coadminister other medicinal products through the same infusion line.

Substitution by any other biological medicinal product requires the consent of the prescribing physician.

The initial dose of Tecentriq must be administered over 60 minutes. If the first infusion is tolerated all subsequent infusions may be administered over 30 minutes.

The recommended dose of Tecentriq is:

- 840 mg administered by IV infusion every 2 weeks, or
- 1200 mg administered by IV infusion every 3 weeks, or
- 1680 mg administered by IV infusion every 4 weeks.

DISETUJUI OLEH BPOM 8 MEI 2025 ID REG: EREG10043712400408-09

Tecentriq monotherapy

Early-stage NSCLC, 1L metastatic NSCLC

Patients should be selected for treatment based on the tumor expression of PD-L1, with no EGFR or ALK genomic tumor aberrations, confirmed by a validated test (see section *3.1.2 Clinical/Efficacy Studies*).

Tecentriq combination therapy

For the use of Tecentriq in combination therapy, please also refer to the full prescribing information for the combination product. Tecentriq should be administered prior to the combination therapy if given on the same day.

1L non-squamous metastatic NSCLC

Tecentriq in combination with bevacizumab, paclitaxel, and carboplatin

During the induction phase, Tecentriq is administered according to its dosing schedules by IV infusion, and bevacizumab, paclitaxel, and carboplatin are administered every 3 weeks for four or six cycles.

The induction phase is followed by a maintenance phase without chemotherapy in which Tecentriq is administered according to its dosing schedules by IV infusion, and bevacizumab is administered every 3 weeks.

1L ES-SCLC

Tecentriq in combination with carboplatin and etoposide

During the induction phase, Tecentriq is administered according to its dosing schedules by IV infusion, and carboplatin and etoposide are administered by IV infusion every three weeks for four cycles. Carboplatin and etoposide are administered on Day 1 of each cycle, and etoposide is also administered on Days 2 and 3.

The induction phase is followed by a maintenance phase without chemotherapy in which Tecentriq is administered according to its dosing schedules by IV infusion.

HCC

Tecentriq in combination with bevacizumab (Avastin)

Tecentriq is administered according to its dosing schedules by IV infusion, and bevacizumab (Avastin) 15 mg/kg is administered every 3 weeks.

Duration of Treatment

Patients are treated with Tecentriq until loss of clinical benefit (see section *3.1.2 Clinical/Efficacy Studies*) or unacceptable toxicity.

Early-stage NSCLC

Patients are treated with Tecentriq for 1 year unless there is disease recurrence or unacceptable toxicity (see section *3.1.2 Clinical/Efficacy Studies*).

Delayed or Missed Doses

If a planned dose of Tecentriq is missed, it should be administered as soon as possible. The schedule of administration should be adjusted to maintain the appropriate interval between doses.

DISETUJUI OLEH BPOM 8 MEI 2025 ID REG: EREG10043712400408-09

Dose Modifications

No dose reductions of Tecentriq are recommended.

Dose Modifications for Immune-Mediated Adverse Reactions

Recommendations for specific adverse drug reactions (see sections *2.4.1 Warnings and Precautions, General* and *2.6.1 Undesirable Effects, Clinical Trials)* are presented in Table 1.

Table 1 Recommended dose modifications for specific adverse drug reactions

Adverse Drug Reaction	Severity	Treatment Modification
Immune-mediated pneumonitis	Grade 2	Withhold[1]
	Grade 3 or 4	Permanently discontinue
Immune-mediated hepatitis in patients without HCC	Grade 2 (ALT or AST > 3x ULN or blood bilirubin > 1.5x ULN for more than 5-7 days)	Withhold[1]
	Grade 3 or 4 (ALT or AST > 5x ULN or blood bilirubin > 3x ULN)	Permanently discontinue
Immune-mediated hepatitis in patients with HCC	If AST/ALT is within normal limits at baseline and increases to > 3x to ≤ 10x ULN If AST/ALT is > 1 to ≤ 3x ULN at baseline and increases to > 5x to ≤ 10x ULN If AST/ALT is > 3x to ≤ 5x ULN at baseline and increases to > 8x to ≤ 10x ULN	Withhold[1]
	If AST/ALT increases to > 10x ULN or total bilirubin increases to > 3x ULN	Permanently discontinue
Immune-mediated colitis	Grade 2 diarrhoea or colitis	Withhold[1]
	Grade 3 diarrhoea or colitis	Withhold[1] Initiate IV corticosteroids and convert to oral corticosteroids after improvement

DISETUJUI OLEH BPOM 8 MEI 2025 ID REG: EREG10043712400408-09

Adverse Drug Reaction	Severity	Treatment Modification
	Grade 4 diarrhoea or colitis	Permanently discontinue
Immune-mediated hypothyroidism	Symptomatic	Withhold[2] Initiate thyroid hormone replacement therapy
Immune-mediated hyperthyroidism	Symptomatic	Withhold[2] Initiate antithyroid therapy as needed
Immune-mediated adrenal insufficiency	Symptomatic	Withhold[1]
Immune-mediated hypophysitis	Grade 2 or 3	Withhold[1]
	Grade 4	Permanently discontinue
Immune-mediated type 1 diabetes	For ≥ Grade 3 hyperglycemia (fasting glucose > 250 mg/dL)	Withhold[2] Initiate insulin
Immune-mediated meningitis, encephalitis, myasthenic syndrome/myasthenia gravis, Guillain-Barré syndrome	All grades	Permanently discontinue
Immune-mediated myelitis	Grade 2,3 or 4	Permanently discontinue
Immune-mediated facial paresis	Grade 1 or 2	Withhold[1]
	Grade 3 or 4	Permanently discontinue
Immune-mediated pancreatitis	Grade 2 or 3 ≥ Grade 3 serum amylase or lipase levels increased (> 2x ULN)	Withhold[1]
	Grade 4 or any grade recurrent pancreatitis	Permanently discontinue
Immune-mediated myocarditis	Grade 2 or above	Permanently discontinue
Immune-mediated myositis	Grade 2 or 3	Withhold[1]
	Grade 4 or Grade 3 recurrent myositis	Permanently discontinue
Immune-mediated nephritis	Grade 2 (creatinine level > 1.5 - 3x baseline or > 1.5 - 3x ULN)	Withhold[1]

DISETUJUI OLEH BPOM 8 MEI 2025 ID REG: EREG10043712400408-09

Adverse Drug Reaction	Severity	Treatment Modification
	Grade 3 (creatinine level > 3x baseline or > 3 - 6x ULN) or 4 (creatinine level > 6x ULN)	Permanently discontinue
Immune-mediated pericardial disorders	Grade 1 pericarditis	Withhold[3]
	Grade 2 or above	Permanently discontinue
Infusion-related reactions	Grade 1 or 2	Reduce rate of infusion or withhold treatment Premedication with antipyretic and antihistamines may be considered for subsequent doses
	Grade 3 or 4	Permanently discontinue
Haemophagocytic lymphohistiocytosis	Suspected haemophagocytic lymphohistiocytosis[4]	Permanently discontinue
Rash/Severe cutaneous adverse reactions	Grade 3 or suspected Stevens-Johnson syndrome (SJS) or toxic epidermal necrolysis (TEN)[3]	Withhold[1]
	Grade 4 or confirmed Stevens-Johnson syndrome (SJS) or toxic epidermal necrolysis (TEN)[3]	Permanently discontinue

[1] Treatment with corticosteroid therapy (1-2 mg/kg/day prednisone or equivalent) should be initiated. Treatment with Tecentriq may be resumed in patients with complete or partial resolution (Grade 0 to 1) within 12 weeks, and after corticosteroids have been reduced to ≤ 10 mg/day oral prednisone or equivalent.
[2] Treatment with Tecentriq may be resumed when symptoms are controlled and the patient is clinically stable.
[3] Conduct a detailed cardiac evaluation to determine the etiology and manage appropriately.
[4] Regardless of severity.

For other immune-mediated reactions, based on the type and severity of the reaction, treatment with Tecentriq should be withheld for Grades 2 or 3 immune-mediated adverse reactions and corticosteroid therapy (1-2 mg/kg/day prednisone or equivalent) should be initiated. If symptoms improve to ≤ Grade 1, taper corticosteroids as clinically indicated. Treatment with Tecentriq may be resumed if the event improves to ≤ Grade 1 within 12 weeks, and corticosteroids have been reduced to ≤ 10 mg oral prednisone or equivalent per day.

Treatment with Tecentriq should be permanently discontinued for Grade 4 immune-mediated adverse reactions, or when unable to reduce corticosteroid dose to the equivalent of ≤ 10 mg prednisone per day within 12 weeks after onset.

DISETUJUI OLEH BPOM 8 MEI 2025 ID REG: EREG10043712400408-09

2.2.1 Special Dosage Instructions

Pediatric use

The safety and efficacy of Tecentriq in children and adolescents below 18 years of age have not been established (see sections *2.5.4 Pediatric Use* and *3.2.5 Pharmacokinetics in Special Populations*).

Geriatric use

Based on a population pharmacokinetic analysis, no dose adjustment of Tecentriq is required in patients ≥ 65 years of age (see sections *2.5.5 Geriatric Use* and *3.2.5 Pharmacokinetics in Special Populations*).

Renal impairment

Based on a population pharmacokinetic analysis, no dose adjustment is required in patients with renal impairment (see section *3.2.5 Pharmacokinetics in Special Populations*).

Hepatic impairment

Based on a population pharmacokinetic analysis, no dose adjustment is required for patients with mild or moderate hepatic impairment. There are no data in patients with severe hepatic impairment (see section *3.2.5 Pharmacokinetics in Special Populations*).

2.3 CONTRAINDICATIONS

Tecentriq is contraindicated in patients with a known hypersensitivity to atezolizumab or any of the excipients.

2.4 WARNINGS AND PRECAUTIONS

2.4.1 General

Haemophagocytic lymphohistiocytosis

Haemophagocytic lymphohistiocytosis (HLH), including fatal cases, has been reported in patients receiving Tecentriq (see section *2.6.1 Undesirable effects, Clinical Trials* and *2.6.2 Postmarketing Experience*). HLH should be considered when the presentation of cytokine release syndrome is atypical or prolonged. Patients should be monitored for clinical signs and symptoms of HLH. Refer to section *2.2. Dosage and Administration* for recommended dose modifications.

Immune-mediated myocarditis

Myocarditis, including fatal cases, has been observed in clinical trials with Tecentriq (see section *2.6.1 Undesirable Effects, Clinical Trials*). Patients should be monitored for signs and symptoms of myocarditis. Myocarditis may also be a clinical manifestation of myositis and should be managed accordingly. Refer to section *2.2 Dosage and Administration* for recommended dose modifications.

Immune-mediated pericardial disorders

Pericardial disorders, including pericarditis, pericardial effusion and cardiac tamponade, some leading to fatal outcomes, have been observed in clinical trials with Tecentriq (see section *2.6.1 Undesirable effects*, *Clinical Trials* and *2.6.2 Postmarketing Experience*). Patients should be monitored for clinical signs and symptoms of pericardial disorders. Refer to section *2.2. Dosage and Administration* for recommended dose modifications.

DISETUJUI OLEH BPOM 8 MEI 2025 ID REG: EREG10043712400408-09

Immune-mediated endocrinopathies

Hypothyroidism, hyperthyroidism, adrenal insufficiency, hypophysitis, and type 1 diabetes mellitus, including diabetic ketoacidosis, have been observed in clinical trials with Tecentriq (see section *2.6.1 Undesirable Effects, Clinical Trials*). Patients should be monitored for clinical signs and symptoms of endocrinopathies. Monitor thyroid function prior to and periodically during treatment with Tecentriq. Consider appropriate management of patients with abnormal thyroid function tests at baseline. Patients with abnormal thyroid function tests who are asymptomatic may receive Tecentriq. Refer to section *2.2 Dosage and Administration* for recommended dose modifications.

Immune-mediated colitis

Cases of diarrhoea or colitis have been observed in clinical trials with Tecentriq (see section *2.6.1 Undesirable Effects, Clinical Trials*). Patients should be monitored for signs and symptoms of colitis. Refer to section *2.2 Dosage and Administration* for recommended dose modifications.

Immune-mediated pancreatitis

Pancreatitis, including increases in serum amylase and lipase levels, has been observed in clinical trials with Tecentriq (see section *2.6.1 Undesirable Effects, Clinical Trials*). Patients should be closely monitored for signs and symptoms that are suggestive of acute pancreatitis. Refer to section *2.2 Dosage and Administration* for recommended dose modifications.

Infusion-related reactions

Infusion-related reactions (IRRs) have been observed in clinical trials with Tecentriq (see section *2.6.1 Undesirable Effects, Clinical Trials*). Refer to section *2.2 Dosage and Administration* for recommended dose modifications.

Immune-mediated hepatitis

Cases of hepatitis, some leading to fatal outcomes, have been observed in clinical trials with Tecentriq (see section *2.6.1 Undesirable Effects, Clinical Trials*). Patients should be monitored for signs and symptoms of hepatitis. Monitor aspartate aminotransferase (AST), alanine aminotransferase (ALT) and bilirubin prior to and periodically during treatment with Tecentriq. Consider appropriate management of patients with abnormal liver function tests (LFTs) at baseline. Refer to section *2.2 Dosage and Administration* for recommended dose modifications.

Immune-mediated myositis

Cases of myositis, including fatal cases, have been observed in clinical trials with Tecentriq (see section *2.6.1 Undesirable Effects, Clinical Trials*). Patients should be monitored for signs and symptoms of myositis. Patients with possible myositis should be monitored for signs of myocarditis. Refer to section *2.2 Dosage and Administration* for recommended dose modifications.

Immune-mediated meningoencephalitis

Meningoencephalitis has been observed in clinical trials with Tecentriq (see section *2.6.1 Undesirable Effects, Clinical Trials*). Patients should be monitored for clinical signs and symptoms of meningitis or encephalitis. Refer to section *2.2 Dosage and Administration* for recommended dose modifications.

DISETUJUI OLEH BPOM 8 MEI 2025 ID REG: EREG10043712400408-09

Immune-mediated neuropathies

Myasthenic syndrome/myasthenia gravis or Guillain-Barré syndrome, which may be life-threatening, and facial paresis were observed in patients receiving Tecentriq (see section *2.6.1 Undesirable Effects, Clinical Trials*). Patients should be monitored for symptoms of motor and sensory neuropathy. Refer to section *2.2 Dosage and Administration* for recommended dose modifications.

Immune-mediated myelitis

Myelitis has been observed in clinical trials with Tecentriq (see section *2.6.1 Undesirable effects, Clinical Trials* and *2.6.2 Postmarketing Experience*). Patients should be closely monitored for signs and symptoms that are suggestive of myelitis. Refer to section *2.2. Dosage and Administration* for recommended dose modifications.

Immune-mediated nephritis

Nephritis has been observed in clinical trials with Tecentriq (see section *2.6.1 Undesirable Effects, Clinical Trials*). Patients should be monitored for changes in renal function. Refer to section *2.2 Dosage and Administration* for recommended dose modifications.

Immune-mediated pneumonitis

Cases of pneumonitis, including fatal cases, have been observed in clinical trials with Tecentriq (see section *2.6.1 Undesirable Effects, Clinical Trials*). Patients should be monitored for signs and symptoms of pneumonitis. Refer to section *2.2 Dosage and Administration* for recommended dose modifications.

Immune-mediated severe cutaneous adverse reactions

Immune-mediated severe cutaneous adverse reactions (SCARs), including cases of Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN), have been reported in patients receiving Tecentriq. Patients should be monitored for suspected severe skin reactions and other causes should be excluded. Based on the severity of the adverse reaction, Tecentriq should be withheld for Grade 3 skin reactions until recovery to Grade ≤ 1 or permanently discontinued for Grade 4 skin reactions, and corticosteroids should be administered (see section *2.2 Dosage and Administration*).

For suspected SCARs, patients should be referred to a specialist for further diagnosis and management. Tecentriq should be withheld for patients with suspected SJS or TEN. For confirmed SJS or TEN, Tecentriq should be permanently discontinued.

Caution should be used when considering the use of Tecentriq in a patient who has previously experienced a severe or life-threatening skin adverse reaction on prior treatment with other immune-stimulatory anticancer agents.

Special populations

Patients with the following conditions were excluded from clinical trials: a history of autoimmune disease, history of pneumonitis, active brain metastatis, HIV, hepatitis B or hepatitis C infection.

Patients who were administered a live, attenuated vaccine within 28 days prior to enrollment; systemic immunostimulatory agents within 4 weeks or systemic immunosuppressive medicinal products within 2 weeks prior to study entry were excluded from clinical trials.

DISETUJUI OLEH BPOM 8 MEI 2025 ID REG: EREG10043712400408-09

Embryo-fetal toxicity

Based on the mechanism of action, the use of Tecentriq may cause fetal harm. Animal studies have demonstrated that inhibition of the PD-L1/PD-1 pathway can lead to increased risk of immune-mediated rejection of the developing fetus resulting in fetal death.

Pregnant women should be advised of the potential risk to the fetus. Women of childbearing potential should be advised to use highly effective contraception during treatment with Tecentriq and for 5 months after the last dose (see sections *2.5.1 Females and Males of Reproductive Potential* and *3.3.4 Reproductive Toxicity*).

2.4.2 Drug Abuse and Dependence

No data to report.

2.4.3 Ability to Drive and Use Machines

No studies on the effects on the ability to drive and to use machines have been performed.

2.5 USE IN SPECIAL POPULATIONS

2.5.1 Females and Males of Reproductive Potential

Fertility

Based on animal studies, Tecentriq may impair fertility in females of reproductive potential while receiving treatment (see section *3.3.3 Impairment of Fertility*).

Contraception

Female patients of childbearing potential should use highly effective contraception and take active measures to avoid pregnancy while undergoing Tecentriq treatment and for at least 5 months after the last dose (see sections *2.4.1 Warnings and Precautions, General* and *3.3.4 Reproductive Toxicity*).

2.5.2 Pregnancy

There are no clinical studies of Tecentriq in pregnant women. Tecentriq is not recommended during pregnancy unless the potential benefit for the mother outweighs the potential risk to the fetus (see section *3.3.4 Reproductive Toxicity*).

Labor and Delivery

The use of Tecentriq during labor and delivery has not been established.

2.5.3 Lactation

It is not known whether Tecentriq is excreted in human breast milk. No studies have been conducted to assess the impact of Tecentriq on milk production or its presence in breast milk. As the potential for harm to the nursing infant is unknown, a decision must be made to either discontinue breast-feeding or discontinue Tecentriq therapy.

2.5.4 Pediatric Use

Tecentriq is not approved for use in patients under the age of 18 years. The safety and efficacy of Tecentriq in this population has not been established. Tecentriq did not demonstrate clinical benefit in pediatric patients in a clinical trial (see section *3.2.5 Pharmacokinetics in Special Populations*).

DISETUJUI OLEH BPOM 8 MEI 2025 ID REG: EREG10043712400408-09

2.5.5 Geriatric Use

No overall differences in safety or efficacy were observed between patients ≥ 65 years of age and younger patients (see sections *2.2.1 Special Dosage Instructions* and *3.2.5 Pharmacokinetics in Special Populations*).

2.5.6 Renal Impairment

See sections *2.2.1 Special Dosage Instructions* and *3.2.5 Pharmacokinetics in Special Populations*.

2.5.7 Hepatic Impairment

See sections *2.2.1 Special Dosage Instructions* and *3.2.5 Pharmacokinetics in Special Populations*.

2.6 UNDESIRABLE EFFECTS

2.6.1 Clinical Trials

The corresponding frequency category for each adverse drug reaction is based on the following convention: very common (≥ 1/10), common (≥ 1/100 to < 1/10), uncommon (≥ 1/1000 to < 1/100), rare (≥ 1/10000 to < 1/1000), very rare (< 1/10000).

Tecentriq Monotherapy

The safety of Tecentriq monotherapy is based on pooled data in 3178 patients with multiple tumor types, with supporting data from the estimated cumulative exposure in > 13000 patients across all clinical trials. Table 2 summarizes the adverse drug reactions (ADRs) that have been reported in association with the use of Tecentriq.

Table 2 Summary of adverse reactions occurring in patients treated with Tecentriq monotherapy in clinical trials

ADR (MedDRA)	Tecentriq (n=3178)			
System Organ Class	All Grades (%)	Grade 3-4 (%)	Grade 5 (%)	Frequency (All Grades)
Blood and Lymphatic System Disorders				
Thrombocytopenia [n]	116 (3.7%)	27 (0.8%)	0 (0%)	Common
Haemophagocytic lymphohistiocytosis[ff]	1 (< 0.1%)	0 (0%)	1 (< 0.1%)	Rare
Cardiac Disorders				
Myocarditis [a]	-	-	-	Rare
Pericardial disorders[ee, ff]	45 (1.4%)	22 (0.7%)	2 (< 0.1%)	Common
Endocrine Disorders				
Hypothyroidism [b]	164 (5.2%)	6 (0.2%)	0 (0%)	Common
Hyperthyroidism [c]	30 (0.9%)	1 (< 0.1%)	0 (0%)	Uncommon
Adrenal insufficiency [d]	11 (0.3%)	2 (< 0.1%)	0 (0%)	Uncommon
Hypophysitis [y]	2 (< 0.1%)	0 (0%)	0 (0%)	Rare
Diabetes mellitus [e]	10 (0.3%)	6 (0.2%)	0 (0%)	Uncommon

DISETUJUI OLEH BPOM 8 MEI 2025 ID REG: EREG10043712400408-09

ADR (MedDRA)	Tecentriq (n=3178)			
System Organ Class	All Grades (%)	Grade 3-4 (%)	Grade 5 (%)	Frequency (All Grades)
Gastrointestinal Disorders				
Diarrhoea [o]	626 (19.7%)	36 (1.1%)	0 (0%)	Very common
Dysphagia	82 (2.6%)	16 (0.5%)	0 (0%)	Common
Colitis [f]	34 (1.1%)	18 (0.6%)	0 (0%)	Common
Nausea	747 (23.5%)	35 (1.1%)	0 (0%)	Very common
Vomiting	477 (15.0%)	26 (0.8%)	0 (0%)	Very common
Abdominal pain	268 (8.4%)	34 (1.1%)	0 (0%)	Common
Pancreatitis [g]	18 (0.6%)	13 (0.4%)	0 (0%)	Uncommon
Oropharyngeal pain [q]	131 (4.1%)	0 (0%)	0 (0%)	Common
Dry mouth	154 (4.8%)	0 (0%)	0 (0%)	Common
General Disorders and Administration Site Conditions				
Chills	207 (6.5%)	2 (< 0.1%)	0 (0%)	Common
Fatigue	1142 (35.9%)	109 (3.4%)	0 (0%)	Very common
Asthenia	461 (14.5%)	63 (2.0%)	0 (0%)	Very common
Influenza-like illness	186 (5.9%)	1 (< 0.1%)	0 (0%)	Common
Pyrexia	638 (20.1%)	17 (0.5%)	0 (0%)	Very common
Infusion-related reaction [h]	34 (1.1%)	5 (0.2%)	0 (0%)	Common
Hepatobiliary Disorders				
ALT increased	167 (5.3%)	46 (1.4%)	0 (0%)	Common
AST increased	180 (5.7%)	46 (1.4%)	0 (0%)	Common
Hepatitis [i]	62 (2.0%)	25 (0.8%)	2 (< 0.1%)	Common
Immune System Disorders				
Hypersensitivity	36 (1.1%)	3 (< 0.1%)	0 (0%)	Common
Infections and Infestations				
Urinary tract infection [p]	368 (11.6%)	86 (2.7%)	0 (0%)	Very common
Investigations				
Blood creatine phosphokinase increased	6 (0.2%)	3 (< 0.1%)	0 (0%)	Uncommon
Metabolism and Nutrition Disorders				
Decreased appetite	810 (25.5%)	35 (1.1%)	0 (0%)	Very common
Hypokalemia [v]	142 (4.5%)	33 (1.0%)	0 (0%)	Common
Hyponatremia [w]	171 (5.4%)	98 (3.1%)	0 (0%)	Common
Hyperglycemia	103 (3.2%)	32 (1.0%)	0 (0%)	Common

DISETUJUI OLEH BPOM 8 MEI 2025 ID REG: EREG10043712400408-09

ADR (MedDRA)	Tecentriq (n=3178)			
System Organ Class	All Grades (%)	Grade 3-4 (%)	Grade 5 (%)	Frequency (All Grades)
Musculoskeletal and Connective Tissue Disorders				
Arthralgia	441 (13.9%)	23 (0.7%)	0 (0%)	Very common
Back pain	487 (15.3%)	52 (1.6%)	0 (0%)	Very common
Musculoskeletal pain [r]	489 (15.4%)	36 (1.1%)	0 (0%)	Very common
Myositis [t, u]	13 (0.4%)	5 (0.2%)	0 (0%)	Uncommon
Nervous System Disorders				
Headache	352 (11.1%)	10 (0.3%)	0 (0%)	Very common
Peripheral neuropathy [ii]	156 (4.9%)	5 (0.2%)	0 (0%)	Common
Guillain-Barré syndrome [j]	5 (0.2%)	4 (0.1%)	0 (0%)	Uncommon
Meningoencephalitis [k]	14 (0.4%)	6 (0.2%)	0 (0%)	Uncommon
Myasthenic syndrome [z]	1 (< 0.1%)	0 (0%)	0 (0%)	Rare
Facial paresis[ff]	1 (< 0.1%)	0 (0%)	0 (0%)	Rare
Myelitis[ff]	1 (< 0.1%)	1 (< 0.1%)	0 (0%)	Rare
Renal and Urinary Disorders				
Blood creatinine increased [aa]	171 (5.4%)	14 (0.4%)	0 (0%)	Common
Nephritis [s]	3 (< 0.1%)	1 (< 0.1%)	0 (0%)	Rare
Respiratory, Thoracic, and Mediastinal Disorders				
Cough	660 (20.8%)	9 (0.3%)	0 (0%)	Very common
Dyspnoea	651 (20.5%)	117 (3.7%)	1 (< 0.1%)	Very common
Hypoxia [x]	75 (2.4%)	36 (1.1%)	0 (0%)	Common
Pneumonitis [l]	87 (2.7%)	27 (0.8%)	1 (< 0.1%)	Common
Nasopharyngitis [bb]	280 (8.8%)	0 (0%)	0 (0%)	Common
Skin and Subcutaneous Tissue Disorders				
Rash [m]	613 (19.3%)	33 (1.1%)	0 (0%)	Very common
Pruritus	400 (12.6%)	7 (0.2%)	0 (0%)	Very common
Dry skin [hh]	199 (6.3%)	2 (< 0.1%)	0 (0%)	Common
Psoriatic conditions [cc]	19 (0.6%)	2 (< 0.1%)	0 (0%)	Uncommon
Severe cutaneous adverse reactions [dd]	22 (0.7%)	3 (< 0.1%)	1 (< 0.1%)	Uncommon
Vascular Disorders				
Hypotension	102 (3.2%)	20 (0.6%)	0 (0%)	Common

DISETUJUI OLEH BPOM 8 MEI 2025 ID REG: EREG10043712400408-09

a. Reported in studies outside the pooled dataset. The frequency is based on the program-wide exposure. Includes reports of autoimmune myocarditis, immune-mediated myocarditis.
b. Includes reports of hypothyroidism, blood thyroid stimulating hormone increased, blood thyroid stimulating hormone decreased, thyroiditis, autoimmune hypothyroidism, euthyroid sick syndrome, myxoedema, thyroid function test abnormal, thyroiditis acute, thyroxine decreased
c. Includes reports of hyperthyroidism, Basedow's disease, endocrine ophthalmopathy, exophthalmos
d. Includes reports of adrenal insufficiency, primary adrenal insufficiency
e. Includes reports of diabetes mellitus, type 1 diabetes mellitus and diabetic ketoacidosis and ketoacidosis
f. Includes reports of colitis, autoimmune colitis, colitis ischaemic, colitis microscopic, colitis ulcerative, immune-mediated enterocolitis (cases of immune-mediated enterocolitis have been reported in studies outside the pooled dataset)
g. Includes reports of pancreatitis, autoimmune pancreatitis, pancreatitis acute, lipase increased and amylase increased
h. includes infusion-related reaction and cytokine release syndrome
i. Includes reports of ascites, autoimmune hepatitis, hepatocellular injury, hepatitis, hepatitis acute, hepatotoxicity, liver disorder, drug-induced liver injury, hepatic failure, hepatic steatosis, hepatic lesion, esophageal varices hemorrhage, varices esophageal
j. Includes reports of Guillain-Barré syndrome and demyelinating polyneuropathy
k. Includes reports of encephalitis, meningitis, photophobia
l. Includes reports of pneumonitis, lung infiltration, bronchiolitis, interstitial lung disease, radiation pneumonitis
m. Includes reports of rash, rash maculo-papular, erythema, rash pruritic, dermatitis acneiform, eczema, dermatitis, rash erythematous, skin ulcer, rash papular, folliculitis, rash macular, skin exfoliation, rash pustular, furuncle, acne, drug eruption, palmar-plantar erythrodysaesthesia syndrome, seborrhoeic dermatitis, dermatitis allergic, erythema of eyelid, skin toxicity, eyelid rash, fixed eruption, rash papulosquamous, rash vesicular, blister, lip blister, pemphigoid, oral blood blister
n. Includes reports of immune thrombocytopenia, thrombocytopenia and platelet count decreased
o. Includes reports of diarrhoea, frequent bowel movements, and gastrointestinal hypermotility
p. Includes reports of urinary tract infection, cystitis, pyelonephritis, Escherichia urinary tract infection, pyelonephritis acute, urinary tract infection bacterial, kidney infection, urinary tract infection fungal, urinary tract infection pseudomonal
q. Includes reports of oropharyngeal pain, throat irritation, oropharyngeal discomfort
r. Includes reports of musculoskeletal pain, myalgia, bone pain
s. Includes reports of nephritis and Henoch-Schonlein Purpura nephritis
t. Includes reports of myositis, rhabdomyolysis, polymyalgia rheumatica, dermatomyositis, muscle abscess, myoglobin urine present
u. Fatal cases have been reported in studies outside the pooled dataset
v. Includes reports of hypokalemia and blood potassium decreased
w. Includes reports of hyponatremia and blood sodium decreased
x. Includes reports of hypoxia, oxygen saturation decreased, PO_2 decreased
y. Includes reports of hypophysitis and temperature regulation disorder
z. Includes report of myasthenia gravis
aa. Includes reports of blood creatinine increased and hypercreatininaemia
bb. Includes reports of nasopharyngitis, nasal congestion and rhinorrhoea
cc. Includes reports of dermatitis psoriasiform and psoriasis
dd. Includes reports of dermatitis bullous, exfoliative rash, erythema multiforme, dermatitis exfoliative generalised, toxic skin eruption, toxic epidermal necrolysis
ee. Includes reports of pericarditis, pericardial effusion, cardiac tamponade and pericarditis constrictive
ff. Reported from postmarketing experience outside the pooled dataset. The frequency is based on the program-wide exposure.
hh. Includes reports of dry skin, xerosis.
ii. Includes reports of neuropathy peripheral, peripheral sensory neuropathy, polyneuropathy, peripheral motor neuropathy, toxic neuropathy, peripheral sensorimotor neuropathy, autoimmune neuropathy, axonal neuropathy, brachial plexopathy, lumbosacral plexopathy, neuralgic amyotrophy, and neuritis

Tecentriq combination therapy

Additional ADRs identified in clinical trials (not reported in monotherapy trials) associated with the use of Tecentriq in combination therapy across multiple indications are summarized in Table 3. ADRs with a clinically relevant difference when compared to monotherapy (refer to *Table 2*) are also presented.

DISETUJUI OLEH BPOM 8 MEI 2025 ID REG: EREG10043712400408-09

Table 3 Summary of adverse reactions occurring in patients treated with Tecentriq combination therapy in clinical trials

ADR (MedDRA)	Tecentriq + Combination Treatments (n=4371)			
System Organ Class	All Grades (%)	Grade 3-4 (%)	Grade 5 (%)	Frequency (All Grades)
Blood and Lymphatic System Disorders				
Anemia[*]	1608 (36.8%)	631 (14.4%)	0 (0%)	Very common
Lymphopenia[*, k]	145 (3.3%)	63 (1.4%)	0 (0%)	Common
Neutropenia[*,a]	1565 (35.8%)	1070 (24.5%)	6 (0.1%)	Very common
Thrombocytopenia[*,‡, b]	1211 (27.7%)	479 (11.0%)	1 (< 0.1%)	Very common
Leukopenia[*, i]	571 (13.1%)	245 (5.6%)	0 (0%)	Very common
Endocrine Disorders				
Hypothyroidism[*,‡,c]	586 (13.4%)	9 (0.2%)	0 (0%)	Very common
Hyperthyroidism[‡]	193 (4.4%)	7 (0.2%)	0 (0%)	Common
Adrenal insufficiency[‡,d]	40 (0.9%)	8 (0.2%)	1 (< 0.1%)	Uncommon
Hypophysitis[‡,e]	13 (0.3%)	5 (0.1%)	0 (0%)	Uncommon
Gastrointestinal Disorders				
Constipation[*]	1123 (25.7%)	24 (0.5%)	0 (0%)	Very common
Stomatitis[*]	351 (8.0%)	23 (0.5%)	0 (0%)	Common
General Disorders and Administration Site Conditions				
Oedema peripheral*	451 (10.3%)	11 (0.3%)	0 (0%)	Very common
Infections and Infestations				
Lung infection[*,h]	564 (12.9%)	226 (5.2%)	26 (0.6%)	Very common
Investigations				
Blood alkaline phosphatase increased	200 (4.6%)	26 (0.6%)	0 (0%)	Common
Metabolism and Nutrition Disorders				
Hypomagnesemia[*, j]	403 (9.2%)	22 (0.5%)	0 (0%)	Common
Nervous System Disorders				
Dizziness[*]	408 (9.3%)	9 (0.2%)	0 (0%)	Common
Dysgeusia[*]	269 (6.2%)	0 (0.0%)	0 (0%)	Common

DISETUJUI OLEH BPOM 8 MEI 2025 ID REG: EREG10043712400408-09

ADR (MedDRA)	Tecentriq + Combination Treatments (n=4371)			
System Organ Class	All Grades (%)	Grade 3-4 (%)	Grade 5 (%)	Frequency (All Grades)
Peripheral neuropathy*,f	976 (22.3%)	104 (2.4%)	0 (0%)	Very common
Syncope*	68 (1.6%)	36 (0.8%)	0 (0%)	Common
Renal and Urinary Disorders				
Nephritis‡, l	23 (0.5%)	15 (0.3%)	0 (0%)	Uncommon
Proteinuria*,g	359 (8.2%)	61 (1.4%)	0 (0%)	Common
Respiratory, Thoracic and Mediastinal Disorders				
Dysphonia*	236 (5.4%)	4 (< 0.1%)	0 (0%)	Common
Nasopharyngitis[o]	442 (10.1%)	1 (< 0.1%)	0 (0%)	Very common
Skin and Subcutaneous Tissue Disorders				
Alopecia [n]	1152 (26.4%)	3 (< 0.1%)	0 (0%)	Very common
Severe cutaneous adverse reactions [p]	27 (0.6 %)	8 (0.2 %)	0 (0%)	Uncommon
Vascular Disorders				
Hypertension*, m	611 (14.0%)	258 (5.9%)	0 (0%)	Very common

∗ ADR occurring at a frequency difference of ≥ 5% (All grades) or ≥ 2% (Grades 3-4) compared to the control arm

‡ Observed rate in the combination represents a clinically relevant difference in comparison to Tecentriq monotherapy

a. Includes reports of neutropenia, neutrophil count decreased, febrile neutropenia, neutropenic sepsis and granulocytopenia

b. Includes reports of immune thrombocytopenia, thrombocytopenia and platelet count decreased

c. Includes reports of hypothyroidism, blood thyroid stimulating hormone increased, blood thyroid stimulating hormone decreased, autoimmune thyroiditis, goitre, thyroiditis, thyroxine free decreased, tri−iodothyronine free decreased, thyroid disorder, thyroxine free increased, thyroxine increased, tri−iodothyronine decreased, tri-iodothyronine free increased, blood thyroid stimulating hormone abnormal, euthyroid sick syndrome, myxoedema coma, thyroid function test abnormal, thyroxine decreased, tri-iodothyronine abnormal, silent thyroiditis and thyroiditis chronic

d. Includes reports of adrenal insufficiency, cortisol decreased, adrenocortical insufficiency acute, secondary adrenocortical insufficiency, adrenocorticotropic hormone stimulation test abnormal, Addison's disease, adrenalitis and adrenocorticotropic hormone deficiency

e. Includes reports of hypophysitis and temperature regulation disorder

f. Includes reports of neuropathy peripheral, peripheral sensory neuropathy, polyneuropathy, peripheral motor neuropathy, toxic neuropathy, autoimmune neuropathy, neuralgic amyotrophy, peripheral sensorimotor neuropathy, axonal neuropathy, brachial plexopathy, lumbosacral plexopathy and neuritis

g. Includes reports of proteinuria, protein urine present, haemoglobinuria, nephrotic syndrome, urine abnormality and albuminuria

h. Includes reports of pneumonia, bronchitis, lower respiratory tract infection, tracheobronchitis, infective exacerbation of chronic obstructive airways disease, infectious pleural effusion, paracancerous pneumonia, atypical pneumonia, lung abscess, pleural infection and pyopneumothorax

i. Includes reports of white blood cell count decreased and leukopenia

j. Includes reports of hypomagnesemia and blood magnesium decreased

k. Includes reports of lymphopenia and lymphocyte count decreased

l. Includes reports of nephritis, tubulointerstitial nephritis, autoimmune nephritis, nephritis allergic, glomerulonephritis, nephrotic syndrome and mesangioproliferative glomerulonephritis

m. Includes reports of hypertension, blood pressure increased, hypertensive crisis, blood pressure systolic increased, diastolic hypertension, blood pressure inadequately controlled and retinopathy hypertensive

n. Includes reports of alopecia, madarosis, alopecia areata, alopecia totalis and hypotrichosis

o. Includes reports of nasopharyngitis, nasal congestion and rhinorrhoea

p. Includes reports of dermatitis bullous, exfoliative rash, erythema multiforme, dermatitis exfoliative generalised, toxic skin eruption, Stevens-Johnson syndrome (SJS), drug reaction with eosinophilia and systemic symptoms (DRESS), toxic

DISETUJUI OLEH BPOM 8 MEI 2025 ID REG: EREG10043712400408-09

epidermal necrolysis (TEN), and cutaneous vasculitis (cases of SJS and DRESS have been reported in studies outside the pooled dataset)

Additional information for selected adverse reactions

The data below reflect information for significant adverse reactions for Tecentriq monotherapy. Details for the significant adverse reactions for Tecentriq when given in combination are presented if clinically relevant differences were noted in comparison to Tecentriq monotherapy. See section *2.4.1 Warnings and Precautions, General* for management of the following:

Haemophagocytic lymphohistiocytosis

Haemophagocytic lymphohistiocytosis (HLH) occurred in < 0.1% (1/3178) of patients who received Tecentriq monotherapy. The time to onset was 1.6 months. The duration was 1.4 months. HLH led to discontinuation of Tecentriq in 1 (< 0.1%) patient. The patient did not require the use of corticosteroids.

Immune-mediated pericardial disorders

Pericardial disorders occurred in 1.4% (45/3178) of patients who received Tecentriq monotherapy. The median time to onset was 1.4 months (range 0.2 to 17.5 months). The median duration was 1.4 months (range 0 to 19.3 months). Pericardial disorders led to discontinuation of Tecentriq in 3 (< 0.1%) patients. Pericardial disorders requiring the use of corticosteroids occurred in 0.2% (7/3178) patients.

Immune-mediated endocrinopathies

Thyroid Disorders

Hypothyroidism occurred in 5.2% (164/3178) of patients who received Tecentriq monotherapy. The median time to onset was 4.9 months (range 0 to 31.3 months).

Hyperthyroidism occurred in 0.9% (30/3178) of patients who received Tecentriq monotherapy. The median time to onset was 2.1 months (range: 0.7 to 15.7 months). The median duration was 2.6 months (range: 0+ to 17.1+ months; + denotes a censored value).

Adrenal Insufficiency

Adrenal insufficiency occurred in 0.3% (11/3178) of patients who received Tecentriq monotherapy. The median time to onset was 5.5 months (range: 0.1 to 19.0 months). The median duration was 16.8 months (range: 0 to 16.8 months). Adrenal insufficiency led to discontinuation of Tecentriq in 1 (< 0.1%) patient. Adrenal insufficiency requiring the use of corticosteroids occurred in 0.3% (9/3178) of patients receiving Tecentriq.

Hypophysitis

Hypophysitis occurred in < 0.1% (2/3178) of patients who received Tecentriq monotherapy. The median time to onset was 7.2 months (range: 0.8 to 13.7 months). One patient required the use of corticosteroids and treatment with Tecentriq was discontinued.

Hypophysitis occurred in 0.8% (3/393) of patients who received Tecentriq with bevacizumab, paclitaxel, and carboplatin. The median time to onset was 7.7 months (range: 5.0 to 8.8 months). Two patients required the use of corticosteroids. Hypophysitis lead to the discontinuation of treatment in one patient.

DISETUJUI OLEH BPOM 8 MEI 2025 ID REG: EREG10043712400408-09

Diabetes Mellitus

Diabetes mellitus occurred in 0.3% (10/3178) of patients who received Tecentriq monotherapy. The median time to onset was 4.2 months (range 0.1 to 9.9 months). The median duration was 1.6 months (range: 0.1 to 15.2+ months; + denotes a censored value). Diabetes mellitus led to the discontinuation of Tecentriq in 3 (< 0.1%) patients.

Immune-mediated colitis

Colitis occurred in 1.1% (34/3178) of patients who received Tecentriq. The median time to onset was 4.7 months (range 0.5 to 17.2 months). The median duration was 1.2 months (range: 0.1 to 17.8+ months; + denotes a censored value). Colitis led to discontinuation of Tecentriq in 8 (0.3%) patients. Colitis requiring the use of corticosteroids occurred in 0.6% (19/3178) of patients receiving Tecentriq.

Immune-mediated pancreatitis

Pancreatitis, including amylase increased and lipase increased, occurred in 0.6% (18/3178) of patients who received Tecentriq monotherapy. The median time to onset was 5.0 months (range: 0.3 to 16.9 months). The median duration was 0.8 months (range: 0.1 to 12.0+ months; + denotes a censored value). Pancreatitis led to discontinuation of Tecentriq in 3 (< 0.1%) patient. Pancreatitis requiring the use of corticosteroids occurred in 0.1% (4/3178) of patients receiving Tecentriq.

Immune-mediated hepatitis

Hepatitis occurred in 2.0% (62/3178) of patients who received Tecentriq monotherapy. Of the 62 patients, two events were fatal. The median time to onset was 1.5 months (range 0.2 to 18.8 months). The median duration was 2.1 months (range: 0 to 22.0+ months; + denotes a censored value). Hepatitis led to discontinuation of Tecentriq in 6 (0.2%) patients. Hepatitis requiring the use of corticosteroids occurred in 0.6% (18/3178) of patients receiving Tecentriq.

Immune-mediated myositis

Myositis occurred in 0.4% (13/3178) of patients who received Tecentriq monotherapy. The median time to onset was 5.1 months (range: 0.7 to 11.0 months). The median duration was 5.0 months (range 0.7 to 22.6+ months, + denotes a censored value). Myositis led to discontinuation of Tecentriq in 1 (< 0.1%) patient. Myositis requiring the use of corticosteroids occurred in 0.2% (7/3178) of patients receiving Tecentriq.

Immune-mediated meningoencephalitis

Meningoencephalitis occurred in 0.4% (14/3178) of patients who received Tecentriq monotherapy. The median time to onset was 0.5 months (range 0 to 12.5 months). The median duration was 0.7 months (range 0.2 to 14.5+ months; + denotes a censored value). Meningoencephalitis requiring the use of corticosteroids occurred in 0.2% (6/3178) of patients receiving Tecentriq and led to discontinuation of Tecentriq in 4 (0.1%) patients.

Immune-mediated neuropathies

Guillain-Barré syndrome and demyelinating polyneuropathy

Guillain-Barré syndrome and demyelinating polyneuropathy, occurred in 0.2% (5/3178) of patients who received Tecentriq monotherapy. The median time to onset was 7.0 months (range: 0.6 to 8.1 months). The median duration was 8.0 months (0.6 to 8.3+ months; + denotes a censored value). Guillain-Barré syndrome led to the discontinuation of Tecentriq

DISETUJUI OLEH BPOM 8 MEI 2025 ID REG: EREG10043712400408-09

in 1 (< 0.1%) patient. Guillain-Barré syndrome requiring the use of corticosteroids occurred in < 0.1% (2/3178) of patients receiving Tecentriq.

Immune-mediated facial paresis

Facial Paresis occurred in < 0.1% (1/3178) of patients who received Tecentriq monotherapy. The time to onset was 0.95 months. The duration was 1.1 months. The event did not require the use of corticosteroids and the event did not lead to discontinuation of Tecentriq.

Immune-mediated myelitis

Myelitis occurred in < 0.1% (1/3178) of patients who received Tecentriq monotherapy. The ime to onset was 0.76 months. The event required the use of corticosteroids but did not lead to discontinuation of Tecentriq.

Immune-mediated nephritis

Nephritis, occurred in < 0.1% (3/3178) of patients who received Tecentriq monotherapy. The median time to onset was 13.1 months (range: 9.0 to 17.5 months). The median duration was 2.8 months (range 0.5 to 9.5+ months; + denotes a censored value). Nephritis led to discontinuation of Tecentriq in 2 (< 0.1%) patients. One patient required the use of corticosteroids.

Immune-mediated pneumonitis

Pneumonitis occurred in 2.7% (87/3178) of patients who received Tecentriq monotherapy. Of the 87 patients, one event was fatal. The median time to onset was 3.4 months (range: 0.1 to 24.8 months). The median duration was 1.4 months (range 0 to 21.2+ months; + denotes a censored value). Pneumonitis led to discontinuation of Tecentriq in 12 (0.4%) patients. Pneumonitis requiring the use of corticosteroids occurred in 1.6% (51/3178) of patients receiving Tecentriq.

Immune-mediated severe cutaneous adverse reactions

Severe cutaneous adverse reactions (SCARs) occurred in 0.7% (22/3178) of patients who received Tecentriq monotherapy. The median time to onset was 5.9 months (range 0.1 to 15.5 months). The median duration was 1.6 months (range 0 to 22.1+ months; + denotes a censored value). SCARs led to discontinuation of Tecentriq in 3 (< 0.1%) patients. SCARs requiring the use of systemic corticosteroids occurred in 0.2% (6/3178) of patients receiving Tecentriq monotherapy.

2.6.2 Postmarketing Experience

The following adverse drug reactions have been identified from post marketing surveillance with TECENTRIQ (see Table 4). Adverse drug reactions from post marketing surveillance are listed by MedDRA system organ class.

DISETUJUI OLEH BPOM 8 MEI 2025 ID REG: EREG10043712400408-09

Table 4 Adverse Drug Reactions from Postmarketing Surveillance

System Organ Class **ADR (preferred term, MedDRA)**	**Frequency**
Blood and Lymphatic System Disorders	
Haemophagocytic lymphohistiocytosis[a]	Rare
Cardiac Disorders	
Pericardial disorders[a,b]	Common
Nervous System Disorders	
Facial paresis[a]	Rare
Myelitis	Rare
[a]Reported from postmarketing experience outside the pooled dataset. The frequency is based on the program-wide exposure. [b]Includes reports of pericarditis, pericardial effusion, cardiac tamponade and pericarditis constrictive	

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorization of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via:

Pusat Farmakovigilans/MESO Nasional

Direktorat Pengawasan Keamanan, Mutu, dan Ekspor Impor Obat, Narkotika, Psikotropika, dan Zat Adiktif
Badan Pengawas Obat dan Makanan
Address: Jl. Percetakan Negara No. 23, Jakarta Pusat, 10560
Email: pv-center@pom.go.id
Phone: +62-21-4244691 Ext.1079
Website: https://e-meso.pom.go.id/ADR

PT Roche Indonesia

Patient Safety
Email: indonesia.safety@roche.com
Phone: +62 21 3041 3000
Website: https://medinfo.roche.com/id/id.html

DISETUJUI OLEH BPOM 8 MEI 2025 ID REG: EREG10043712400408-09

2.7 OVERDOSE

There is no information on overdose with Tecentriq.

2.8 INTERACTIONS WITH OTHER MEDICINAL PRODUCTS AND OTHER FORMS OF INTERACTION

No formal pharmacokinetic drug-drug interaction studies have been conducted with atezolizumab. Since atezolizumab is cleared from the circulation through catabolism, no metabolic drug-drug interactions are expected.

The use of systemic corticosteroids or immunosuppressants before starting atezolizumab should be avoided because of their potential interference with the pharmacodynamic activity and efficacy of atezolizumab. However, systemic corticosteroids or other immunosuppressants can be used to treat immune-mediated adverse reactions after starting atezolizumab (see section *2.4 Warnings and Precautions*).

3. PHARMACOLOGICAL PROPERTIES AND EFFECTS

3.1 PHARMACODYNAMIC PROPERTIES

3.1.1 Mechanism of Action

Binding of PD-L1 to the PD-1 and B7.1 receptors found on T cells suppresses cytotoxic T cell activity through the inhibition of T cell proliferation and cytokine production. PD-L1 may be expressed on tumor cells and tumor-infiltrating immune cells, and can contribute to the inhibition of the antitumor immune response in the microenvironment.

Atezolizumab is an Fc-engineered humanized immunoglobulin G1 (IgG1) monoclonal antibody that directly binds to PD-L1 and blocks interactions with the PD-1 and B7.1 receptors, releasing PD-L1/PD-1 pathway-mediated inhibition of the immune response, including reactivating the antitumor immune response. Atezolizumab leaves the PD-L2/PD-1 interaction intact. In syngeneic mouse tumor models, blocking PD-L1 activity resulted in decreased tumor growth.

3.1.2 Clinical/Efficacy Studies

UC

IMvigor211

A phase III, open-label, multi-center, international, randomized study, GO29294 (IMvigor211), was conducted to evaluate the efficacy and safety of Tecentriq compared with chemotherapy (investigator's choice of vinflunine, docetaxel, or paclitaxel) in patients with locally advanced or metastatic urothelial carcinoma who progressed during or following a platinum-containing regimen. This study excluded patients who had a history of autoimmune disease; active or corticosteroid-dependent brain metastases; administration of a live, attenuated vaccine within 28 days prior to enrollment; and administration of systemic immunostimulatory agents within 4 weeks or systemic immunosuppressive medicinal product within 2 weeks prior to enrollment. Tumor assessments were conducted every 9 weeks for the first 54 weeks, and every 12 weeks thereafter. Tumor specimens were evaluated prospectively for PD-L1 expression on tumor-infiltrating immune cells (IC) and the results were used to define the PD-L1 expression subgroups for the analyses described below.

A total of 931 patients were enrolled. Patients were randomized (1:1) to receive either Tecentriq or chemotherapy. Randomization was stratified by chemotherapy (vinflunine vs. taxane), PD-L1 expression status on IC (< 5% vs. ≥ 5%), number of prognostic risk factors

DISETUJUI OLEH BPOM 8 MEI 2025 ID REG: EREG10043712400408-09

(0 vs. 1-3), and liver metastases (yes vs. no). Prognostic risk factors included time from prior chemotherapy of < 3 months, ECOG performance status > 0 and hemoglobin < 10 g/dL.

Tecentriq was administered as a fixed dose of 1200 mg by intravenous infusion every 3 weeks. No dose reduction of Tecentriq was allowed. Patients were treated until loss of clinical benefit as assessed by the investigator or unacceptable toxicity. Vinflunine was administered 320 mg/m^2 by intravenous infusion on Day 1 of each 3-week cycle until disease progression or unacceptable toxicity. Paclitaxel was administered 175 mg/m^2 by intravenous infusion over 3 hours on Day 1 of each 3-week cycle until disease progression or unacceptable toxicity. Docetaxel was administered 75 mg/m^2 by intravenous infusion on Day 1 of each 3-week cycle until disease progression or unacceptable toxicity. For all treated patients, the median duration of treatment was 2.8 months for the Tecentriq arm, 2.1 months for the vinflunine and paclitaxel arms and 1.6 months for the docetaxel arm.

The demographic and baseline disease characteristics of the primary analysis population were well balanced between the treatment arms. The median age was 67 years (range: 31 to 88), and 77.1% of patients were male. The majority of patients were white (72.1%), 53.9% of patients within the chemotherapy arm received vinflunine, 71.4% of patients had at least one poor prognostic risk factor and 28.8% had liver metastases at baseline. Baseline ECOG performance status was 0 (45.6%) or 1 (54.4%). Bladder was the primary tumor site for 71.1% of patients and 25.4% of patients had upper tract urothelial carcinoma. There were 24.2% of patients who received only prior platinum-containing adjuvant or neoadjuvant therapy and progressed within 12 months.

The primary efficacy endpoint for IMvigor211 was overall survival (OS). Secondary efficacy endpoints were objective response rate (ORR), progression-free survival (PFS), and duration of response (DOR). OS comparisons between the treatment arm and control arm were tested using a hierarchical fixed-sequence procedure based on a stratified log-rank test at two-sided level of 5% as follows: step 1) PD-L1 expression ≥ 5% subgroup, step 2) PD-L1 expression ≥ 1% subgroup, step 3) all comers. OS results for each of steps 2 and 3 could only be formally tested if the result in the preceding step was statistically significant.

The median survival follow-up was 17 months. Study IMvigor211 did not meet its primary endpoint. In the subset of patients with tumors having PD-L1 expression ≥ 5%, Tecentriq did not demonstrate a statistically significant survival benefit compared to chemotherapy with an OS HR of 0.87 (95% CI: 0.63, 1.21; median OS of 11.1 vs. 10.6 months for Tecentriq and chemotherapy, respectively). The stratified log rank p-value was 0.41. As a consequence, no formal statistical testing was performed for OS in the PD-L1 expression ≥ 1% subgroup or in all comers, and results of those analyses are considered exploratory. The key results in the all comer population are summarized in Table 5. The Kaplan-Meier curve for OS in the all comer population is presented in Figure 1.

Table 5 Summary of efficacy in all comers (IMvigor211)

Efficacy endpoint	**Tecentriq (n=467)**	**Chemotherapy (n=464)**
Primary efficacy endpoint		
OS		
No. of deaths (%)	324 (69.4%)	350 (75.4%)
Median time to events (months)	8.6	8.0
95% CI	7.8, 9.6	7.2, 8.6
Stratified‡ hazard ratio (95% CI)	0.85 (0.73, 0.99)	
12-month OS (%)*	39.2%	32.4%

DISETUJUI OLEH BPOM 8 MEI 2025 ID REG: EREG10043712400408-09

Efficacy endpoint	Tecentriq (n=467)	Chemotherapy (n=464)
Secondary and exploratory endpoints		
Investigator-assessed PFS (RECIST v1.1)		
No. of events (%)	407 (87.2%)	410 (88.4%)
Median duration of PFS (months)	2.1	4.0
95% CI	2.1, 2.2	3.4, 4.2
Stratified hazard ratio (95% CI)	1.10 (0.95, 1.26)	
Investigator-assessed ORR (RECIST v1.1)	n=462	n=461
No. of confirmed responders (%)	62 (13.4%)	62 (13.4%)
95% CI	10.45, 16.87	10.47, 16.91
No. of complete response (%)	16 (3.5%)	16 (3.5%)
No. of partial response (%)	46 (10.0%)	46 (10.0%)
No. of stable disease (%)	92 (19.9%)	162 (35.1%)
Investigator-assessed DOR (RECIST v1.1)	n=62	n=62
Median in months **	21.7	7.4
95% CI	13.0, 21.7	6.1, 10.3

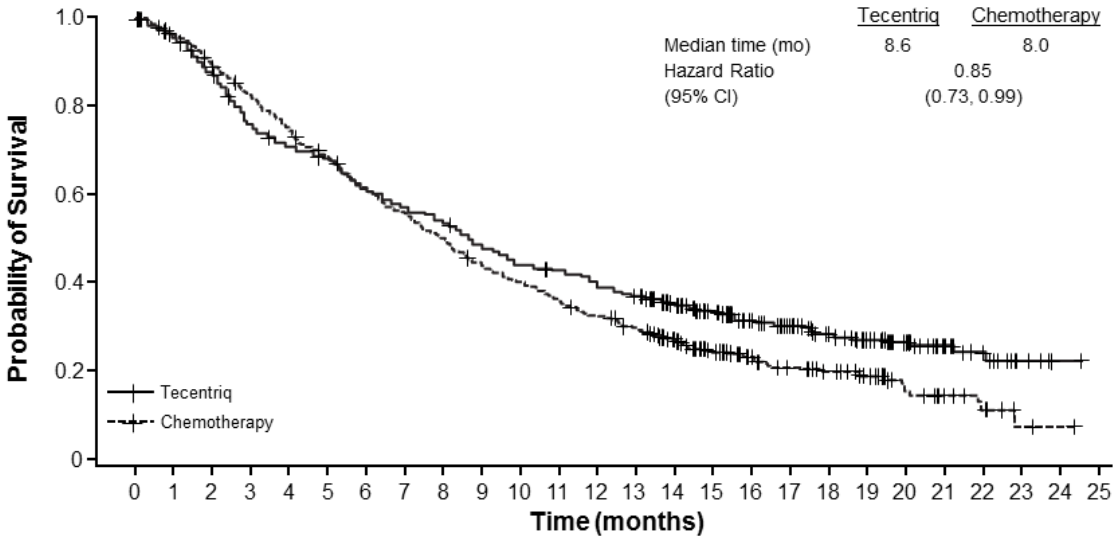
CI=confidence interval; DOR=duration of response; ORR=objective response rate; OS=overall survival; PFS=progression-free survival; RECIST=response evaluation criteria in solid tumors v1.1

* Based on Kaplan-Meier estimate

‡ Stratified by chemotherapy (vinflunine vs. taxane), PD-L1 status on IC (< 5% vs. ≥ 5%), number of prognostic risk factors (0 vs. 1-3), and liver metastases (yes vs. no)

** Responses were ongoing in 63% of responders in the Tecentriq arm and in 21% of responders in the chemotherapy arm

Figure 1 Kaplan-Meier curve for overall survival in all comers (IMvigor211)



No. of Patients at Risk

Tecentriq	467	443	405	348	327	309	280	259	245	218	201	192	177	166	138	113	90	76	59	47	34	20	13	5	1
Chemotherapy	464	428	397	364	330	299	268	244	219	191	175	156	140	126	99	78	60	49	42	30	17	11	7	2	1

DISETUJUI OLEH BPOM 8 MEI 2025 ID REG: EREG10043712400408-09

NSCLC

Early-stage NSCLC

IMpower010

A phase III, open-label, multi-center, randomized study, GO29527 (IMpower010), was conducted to evaluate the efficacy and safety of Tecentriq for the adjuvant treatment of patients with stage IB (tumors ≥ 4 cm) – IIIA NSCLC (per the Union for International Cancer Control/American Joint Committee on Cancer staging system, 7th edition). A total of 1280 enrolled patients had complete tumor resection and were eligible to receive up to 4 cycles of cisplatin-based chemotherapy. The cisplatin-based chemotherapy regimens are described in Table 6.

Table 6 Chemotherapy intravenous treatment regimens in study IMpower010

Adjuvant cisplatin-based chemotherapy Cisplatin 75 mg/m^2 IV on Day 1 of each 21-day cycle with one of the following treatment regimens	Vinorelbine 30 mg/m^2 IV, Day 1 and 8
	Docetaxel 75 mg/m^2 IV, Day 1
	Gemcitabine 1250 mg/m^2 IV, Day 1 and 8
	Pemetrexed 500 mg/m^2 IV, Day 1

After completion of cisplatin-based chemotherapy (up to four cycles), a total of 1005 patients were randomized in a 1:1 ratio to receive Tecentriq (Arm A) or best supportive care (BSC) (Arm B). Tecentriq was administered as a fixed dose of 1200 mg by IV infusion every 3 weeks for 16 cycles unless there was disease recurrence or unacceptable toxicity. Randomization was stratified by sex, stage of disease, histology, and PD-L1 expression.

Patients were excluded if they had a history of autoimmune disease; administration of a live, attenuated vaccine within 28 days prior to randomization; administration of systemic immunostimulatory agents within 4 weeks or systemic immunosuppressive medications within 2 weeks prior to randomization. Tumor assessments were conducted at baseline of the randomization phase and every 4 months for the first year following Cycle 1, Day 1 and then every 6 months until year five, then annually thereafter.

The demographics and baseline disease characteristics were well balanced between the treatment arms. The median age was 62 years (range: 26 to 84), and 67% of patients were male. The majority of patients were white (73%) and 24% were Asian. Most patients were current or previous smokers (78%) and baseline ECOG performance status in patients was 0 (55%) or 1 (44%). Overall, 12% of patients had stage IB, 47% had stage II and 41% had stage IIIA disease. The percentage of patients who had tumors with PD-L1 expression ≥ 1% on TC as measured by the VENTANA PD-L1 (SP263) Assay was 55%.

The primary efficacy outcome measure was disease-free survival (DFS) as assessed by the investigator. DFS was defined as the time from the date of randomization to the date of occurrence of any of the following: first documented recurrence of disease, new primary NSCLC, or death due to any cause, whichever occurred first. A key secondary efficacy outcome measure was overall survival (OS).

At the time of the interim DFS analysis, the study met its primary endpoint and demonstrated a statistically significant and clinically meaningful improvement in DFS in the Tecentriq arm compared with the BSC arm in the PD-L1 ≥ 1% TC stage II - IIIA patient population. The median follow-up time was approximately 32 months. The OS data were immature at the time of the DFS interim analysis with approximately 18.9% of deaths

DISETUJUI OLEH BPOM 8 MEI 2025 ID REG: EREG10043712400408-09

reported in both arms in the PD-L1 ≥ 1% TC stage II - IIIA patient population. An exploratory analysis of OS suggested a trend in favor of Tecentriq over BSC (stratified HR=0.77 [95% CI: 0.51, 1.17]) in this patient population.

The study also demonstrated a statistically significant improvement in DFS for all randomized stage II - IIIA patients (stratified HR: 0.79 [95% CI 0.64, 0.96], p-value 0.0205).

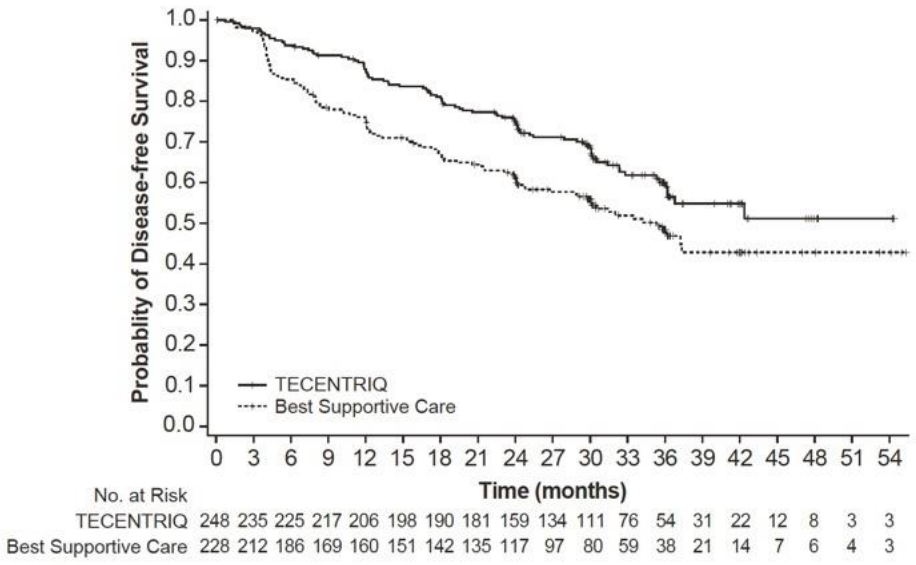
The key efficacy results are summarized in Table 7. The Kaplan-Meier curve for DFS is presented in Figure 2.

Table 7 Summary of efficacy from IMpower010 in PD-L1 expression ≥ 1% TC stage II - IIIA patient population

Efficacy endpoints	**Arm A** (Tecentriq)	**Arm B** (Best supportive care)
Investigator-assessed DFS	n=248	n=228
No. of events (%)	88 (35.5)	105 (46.1)
Median duration of DFS (months)	NE	35.3
95% CI	36.1, NE	29.0, NE
Stratified* hazard ratio (95% CI)	0.66 (0.50, 0.88)	
p-value	0.004	
3 year DFS rate (%)	60.0	48.2

DFS=Disease-free Survival; CI=Confidence Interval; NE=Not Estimable
*Stratified by stage of disease, sex, and histology

Figure 2 Kaplan-Meier plot of disease-free survival in the PD-L1 expression ≥ 1% TC stage II - IIIA patient population



The observed DFS improvement in the Tecentriq arm compared with the BSC arm was consistently shown across the majority of prespecified subgroups in the PD-L1 ≥ 1% TC stage II - IIIA patient population including both non-squamous NSCLC patients

DISETUJUI OLEH BPOM 8 MEI 2025 ID REG: EREG10043712400408-09

(unstratified HR: 0.60 [95% CI: 0.42, 0.84], median DFS 42.3 vs. 30.1 months) and squamous NSCLC patients (unstratified HR: 0.78 [95% CI: 0.47, 1.29], median DFS (NE vs. NE months).

2L NSCLC

OAK

A phase III, open-label, multi-center, international, randomized study, GO28915 (OAK), was conducted to evaluate the efficacy and safety of Tecentriq compared with docetaxel in patients with locally advanced or metastatic NSCLC who have progressed during or following a platinum-containing regimen. A total of 1225 patients were enrolled, with the primary analysis population consisting of the first 850 randomized patients. Eligible patients were stratified by PD-L1 expression status in tumor-infiltrating immune cells (IC), by the number of prior chemotherapy regimens, and by histology. Patients were randomized (1:1) to receive either Tecentriq or docetaxel. This study excluded patients who had a history of autoimmune disease, active or corticosteroid-dependent brain metastases, administration of a live, attenuated vaccine within 28 days prior to enrollment, administration of systemic immunostimulatory agents within 4 weeks or systemic immunosuppressive medications within 2 weeks prior to enrollment. Tumor assessments were conducted every 6 weeks for the first 36 weeks, and every 9 weeks thereafter. Tumor specimens were evaluated prospectively for PD-L1 expression on tumor cells (TC) and IC and the results were used to define the PD-L1 expression subgroups for the analyses described below.

The demographic and baseline disease characteristics of the primary analysis population were well balanced between the treatment arms. The median age was 64 years (range: 33 to 85), and 61% of patients were male. The majority of patients were white (70%). Approximately three-fourths of patients had non-squamous disease (74%), 10% had known EGFR mutation, 0.2% had known ALK rearrangements, 10% had CNS metastases at baseline, and most patients were current or previous smokers (82%). Baseline ECOG performance status was 0 (37%) or 1 (63%). Seventy five percent of patients received only one prior platinum-based therapeutic regimen.

Tecentriq was administered as a fixed dose of 1200 mg by IV infusion every 3 weeks. No dose reduction was allowed. Patients were treated until loss of clinical benefit as assessed by the investigator. Docetaxel was administered 75 mg/m^2 by IV infusion on Day 1 of each 21-day cycle until disease progression. For all treated patients, the median duration of treatment was 2.1 months for the docetaxel arm and 3.4 months for the Tecentriq arm.

The primary efficacy endpoint was OS. The key results of this study with a median survival follow-up of 21 months are summarized in Table 8. Kaplan-Meier curves for OS in the ITT population are presented in Figure 3. Figure 4 summarizes the results of OS in the ITT and PD-L1 subgroups, demonstrating OS benefit with Tecentriq in all subgroups, including those with PD-L1 expression < 1% in TC and IC.

DISETUJUI OLEH BPOM 8 MEI 2025 ID REG: EREG10043712400408-09

Table 8 Summary of efficacy in the primary analysis population (OAK)

Efficacy endpoints	Tecentriq	Docetaxel
Primary efficacy endpoint		
OS		
All comers*	n=425	n=425
No. of deaths (%)	271 (64%)	298 (70%)
Median time to events (months)	13.8	9.6
95% CI	(11.8, 15.7)	(8.6, 11.2)
Stratified‡ hazard ratio (95% CI)	0.73 (0.62, 0.87)	
p-value**	0.0003	
12-month OS (%)	218 (55%)	151 (41%)
18-month OS (%)	157 (40%)	98 (27%)
PD-L1 expression ≥ 1% in TC or IC	n=241	n=222
No. of deaths (%)	151 (63%)	149 (67%)
Median time to events (months)	15.7	10.3
95% CI	(12.6, 18.0)	(8.8, 12.0)
Stratified hazard ratio (95% CI)	0.74 (0.58, 0.93)	
p-value**	0.0102	
12-month OS (%)	58%	43%
18-month OS (%)	44%	29%
Secondary endpoints		
Investigator-assessed PFS (RECIST v1.1)		
All comers*	n=425	n=425
No. of events (%)	380 (89%)	375 (88%)
Median duration of PFS (months)	2.8	4.0
95% CI	(2.6, 3.0)	(3.3, 4.2)
Stratified hazard ratio (95% CI)	0.95 (0.82, 1.10)	
Investigator-assessed ORR (RECIST v1.1)		
All comers	n=425	n=425
No. of responders (%)	58 (14%)	57 (13%)
95% CI	(10.5, 17.3)	(10.3, 17.0)
Investigator-assessed DOR (RECIST v1.1)		
All comers	n=58	n=57
Median in months	16.3	6.2
95% CI	(10.0, NE)	(4.9, 7.6)

CI=confidence interval; DOR=duration of response; IC=tumor-infiltrating immune cells; NE=not estimable; ORR=objective response rate; OS=overall survival; PFS=progression-free survival; RECIST=response evaluation criteria in solid tumors v1.1; TC=tumor cells

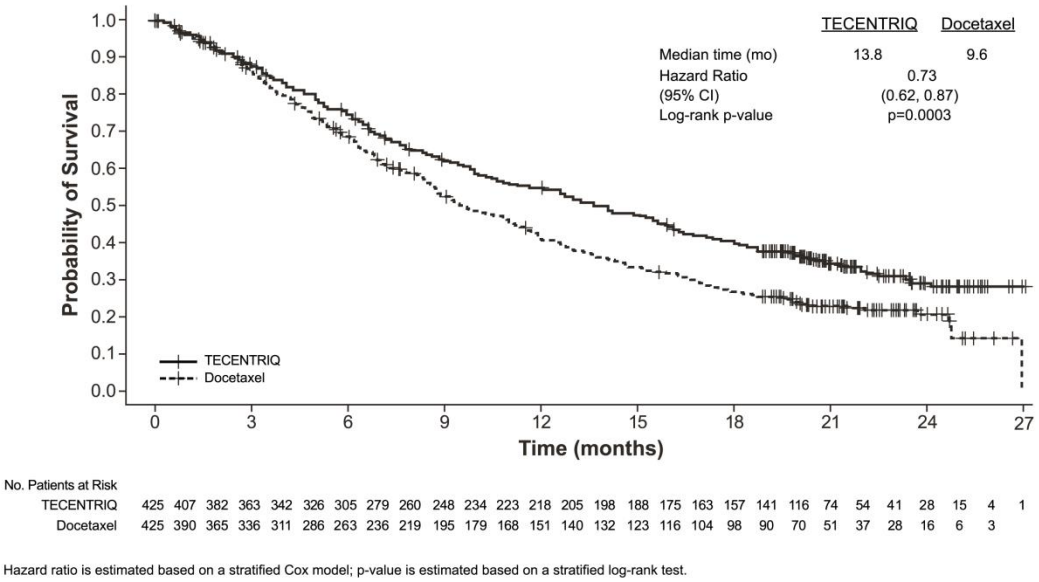
*All comers refer to the primary analysis population consisting of the first 850 randomized patients

‡Stratified by PD-L1 expression in tumor-infiltrating immune cells, the number of prior chemotherapy regimens, and histology

** Based on the stratified log-rank test

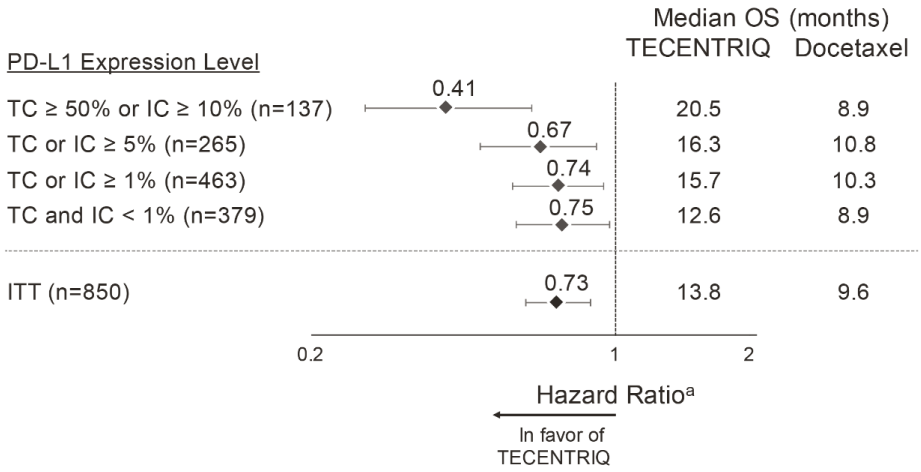
DISETUJUI OLEH BPOM 8 MEI 2025 ID REG: EREG10043712400408-09

Figure 3 Kaplan-Meier plot for overall survival in the primary analysis population (all comers) (OAK)



Hazard ratio is estimated based on a stratified Cox model; p-value is estimated based on a stratified log-rank test.

Figure 4 Forest plot of overall survival by PD-L1 expression in the primary analysis population (OAK)



[a]Stratified HR for ITT and TC or IC ≥ 1%. Unstratified HR for other subgroups

An improvement in OS was observed with Tecentriq compared to docetaxel in both non-squamous NSCLC patients (hazard ratio [HR] of 0.73, 95% CI: 0.60, 0.89; median OS of 15.6 vs. 11.2 months for Tecentriq and docetaxel, respectively) and squamous NSCLC patients (HR of 0.73, 95% CI: 0.54, 0.98; median OS of 8.9 vs. 7.7 months for Tecentriq and docetaxel, respectively). The observed OS improvement was consistently demonstrated across subgroups of patients including those with brain metastases at baseline (HR of 0.54, 95% CI: 0.31, 0.94; median OS of 20.1 vs. 11.9 months for Tecentriq

DISETUJUI OLEH BPOM 8 MEI 2025 ID REG: EREG10043712400408-09

and docetaxel, respectively) and patients who were never smokers (HR of 0.71, 95% CI: 0.47, 1.08; median OS of 16.3 vs. 12.6 months for Tecentriq and docetaxel, respectively). However, patients with EGFR mutations did not show improved OS with Tecentriq compared to docetaxel (HR of 1.24, 95% CI: 0.71, 2.18; median OS of 10.5 vs. 16.2 months for Tecentriq and docetaxel, respectively).

Prolonged time to deterioration of patient-reported pain in chest as measured by the EORTC QLQ-LC13 was observed with Tecentriq compared with docetaxel (HR 0.71, 95% CI: 0.49, 1.05; median not reached in either arm). The time to deterioration in other lung cancer symptoms (i.e. cough, dyspnoea, and arm/shoulder pain) as measured by the EORTC QLQ-LC13 was similar between Tecentriq and docetaxel. The average global health status and functioning scores (i.e. physical, role, social, emotional, and cognitive) as measured by the EORTC QLQ-C30 did not show clinically meaningful deterioration over time for both treatment groups, suggesting maintained health-related quality of life and patient-reported functioning for patients remaining on treatment.

POPLAR

A phase II, multi-center, international, randomized, open-label, controlled study GO28753 (POPLAR), was conducted in patients with locally advanced or metastatic NSCLC. The primary efficacy outcome was overall survival. A total of 287 patients were randomized 1:1 to receive either Tecentriq or docetaxel. Randomization was stratified by PD-L1 expression status in IC, by the number of prior chemotherapy regimens and by histology. An updated analysis with a total of 200 deaths observed and a median survival follow-up of 22 months showed a median OS of 12.6 months in patients treated with Tecentriq, vs. 9.7 months in patients treated with docetaxel (HR of 0.69, 95% CI: 0.52, 0.92). ORR was 15.3% vs. 14.7% and median DOR was 18.6 months vs. 7.2 months for Tecentriq vs. docetaxel, respectively.

1L metastatic non-squamous and squamous NSCLC

IMpower110

A phase III, open-label, multi-center, randomized study, GO29431 (IMpower110), was conducted to evaluate the efficacy and safety of Tecentriq in chemotherapy-naïve patients with metastatic NSCLC, with PD-L1 expression ≥ 1% tumor cell (PD-L1 stained ≥ 1% of tumor cells) or ≥ 1% tumor-infiltrating immune cells (PD-L1 stained tumor-infiltrating immune cells covering ≥ 1% of the tumor area) by the VENTANA PD-L1 (SP142) Assay.

A total of 572 patients were randomized in a 1:1 ratio to receive Tecentriq (Arm A) or chemotherapy (Arm B). Tecentriq was administered as a fixed dose of 1200 mg by IV infusion every 3 weeks until loss of clinical benefit as assessed by the investigator or unacceptable toxicity. The chemotherapy regimens are described in Table 9. Randomization was stratified by sex, ECOG performance status, histology, and PD-L1 tumor expression on tumor cells and tumor-infiltrating immune cells.

Table 9 Chemotherapy intravenous treatment regimens in study IMpower110

Treatment regimen	Induction (Four or six 21-day cycles)	Maintenance (21-day cycles)
B (Non-squamous)	Cisplatin[a] (75 mg/m²) + pemetrexed[a] (500 mg/m²) OR carboplatin[a] (AUC 6) + pemetrexed[b] (500 mg/m²)	Pemetrexed[b, d] (500 mg/m²)
B (Squamous)	Cisplatin[a] (75 mg/m²) + gemcitabine[a,c] (1250 mg/m²) OR carboplatin[a] (AUC 5) + gemcitabine[a,c] (1000 mg/m²)	Best supportive care[d]

DISETUJUI OLEH BPOM 8 MEI 2025 ID REG: EREG10043712400408-09

[a] Cisplatin, carboplatin, pemetrexed and gemcitabine are administered until completion of 4 or 6 cycles, or progressive disease or unacceptable toxicity
[b] Pemetrexed is administered as maintenance regimen every 21 days until progressive disease or unacceptable toxicity
[c] Gemcitabine is administered on Days 1 and 8 of each cycle
[d] No crossover was allowed from the control arm (platinum-based chemotherapy) to the Tecentriq arm (Arm A)

Patients were excluded if they had history of autoimmune disease; administration of a live, attenuated vaccine within 28 days prior to randomization; administration of systemic immunostimulatory agents within 4 weeks or systemic immunosuppressive medications within 2 weeks prior to randomization; active or untreated CNS metastases. Tumor assessments were conducted every 6 weeks for the first 48 weeks following Cycle 1, Day 1 and then every 9 weeks thereafter.

The demographics and baseline disease characteristics in patients with PD-L1 expression ≥ 1% tumor cells or ≥ 1% tumor-infiltrating immune cells who do not have EGFR or ALK genomic tumor aberrations (n=554) were well balanced between the treatment arms. The median age was 64.5 years (range: 30 to 87), and 70% of patients were male. The majority of patients were white (84%) and Asian (14%). Most patients were current or previous smokers (87%) and baseline ECOG performance status in patients was 0 (36%) or 1 (64%). Overall, 69% of patients had non-squamous disease and 31% of patients had squamous disease. The demographics and baseline disease characteristics in patients with high PD-L1 expression (PD-L1 ≥ 50% tumor cells or ≥ 10% tumor-infiltrating immune cells) who do not have EGFR or ALK genomic tumor aberrations (n=205) were generally representative of the broader study population and were balanced between the treatment arms.

The primary endpoint was overall survival (OS). At the time of the interim OS analysis, patients with high PD-L1 expression excluding those with EGFR or ALK genomic tumor aberrations (n=205) demonstrated statistically significant improvement in OS for the patients randomized to Tecentriq (Arm A) as compared with chemotherapy (Arm B). The median survival follow-up time in patients with high PD-L1 expression was 15.7 months. The key results are summarized in Table 10. The Kaplan-Meier curves for OS and PFS in patients with high PD-L1 expression are presented in Figure 5 and 6.

Table 10 Summary of efficacy from IMpower110 in patients with high PD-L1 expression (≥ 50% tumor cells or ≥ 10% tumor-infiltrating immune cells by the VENTANA PD-L1 [SP142] Assay)

Key efficacy endpoints	**Arm A** (Tecentriq)	**Arm B** (Chemotherapy)
Primary endpoint		
OS analysis	n=107	n=98
No. of deaths (%)	44 (41.1%)	57 (58.2%)
Median time to events (months)	20.2	13.1
95% CI	(16.5, NE)	(7.4, 16.5)
Stratified hazard ratio‡ (95% CI)	0.59 (0.40, 0.89)	
p-value‡	0.0106	
12-month OS (%)	64.9	50.6
Secondary endpoints		
Investigator-assessed PFS (RECIST v1.1)	n=107	n=98

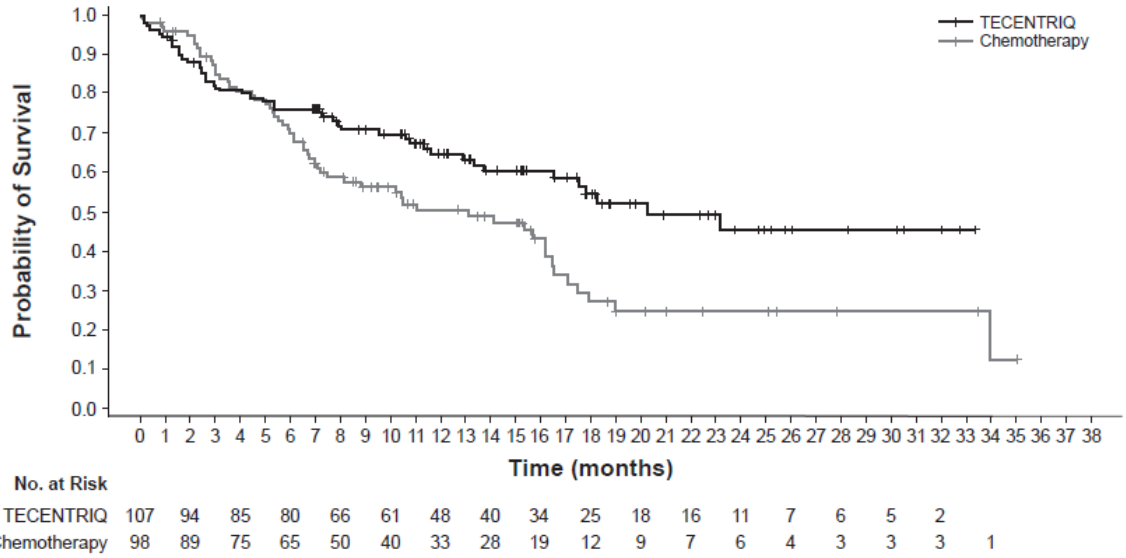
DISETUJUI OLEH BPOM 8 MEI 2025 ID REG: EREG10043712400408-09

Key efficacy endpoints	**Arm A** (Tecentriq)	**Arm B** (Chemotherapy)
No. of events (%)	67 (62.6%)	79 (80.6%)
Median duration of PFS (months)	8.1	5.0
95% CI	(6.8, 11.0)	(4.2, 5.7)
Stratified hazard ratio‡ (95% CI)	0.63 (0.45, 0.88)	
12-month PFS (%)	36.9	21.6
Investigator-assessed ORR (RECIST 1.1)	n=107	n=98
No. of responders (%)	41 (38.3%)	28 (28.6%)
95% CI	(29.1, 48.2)	(19.9, 38.6)
No. of complete response (%)	1 (0.9%)	1 (1.0%)
No. of partial response (%)	40 (37.4%)	27 (27.6%)
Investigator-assessed DOR (RECIST 1.1)	n=41	n=28
Median in months	NE	6.7
95% CI	(11.8, NE)	(5.5, 17.3)

‡ Stratified by sex and ECOG performance status (0 vs. 1)

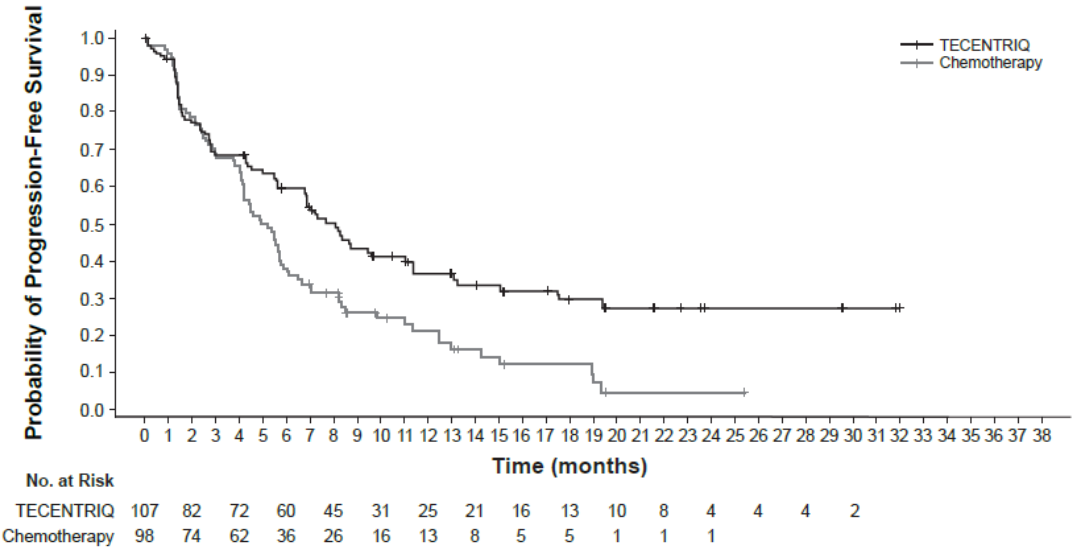
PFS=progression-free survival; RECIST=response evaluation criteria in solid tumors v1.1; CI=confidence interval; ORR=objective response rate; DOR=duration of response; OS=overall survival; NE=not estimable.

Figure 5 Kaplan-Meier plot of overall survival in patients with high PD-L1 expression (≥ 50% tumor cells or ≥ 10% tumor-infiltrating immune cells)



DISETUJUI OLEH BPOM 8 MEI 2025 ID REG: EREG10043712400408-09

Figure 6 Kaplan-Meier plot of progression-free survival in patients with high PD-L1 expression ≥ 50% (tumor cells or ≥ 10% tumor-infiltrating immune cells)



The observed OS improvement in the Tecentriq arm compared with the chemotherapy arm was consistently demonstrated across subgroups in patients with high PD-L1 expression including both non-squamous NSCLC patients (HR: 0.62 [95% CI: 0.40, 0.96], median OS 20.2 vs. 10.5 months) and squamous NSCLC patients (HR: 0.56 [95% CI: 0.23, 1.37]) median OS NE vs. 15.3 months). The data for patients ≥ 75 years old and patients who were never smokers are too limited to draw conclusions in these subgroups.

Additional prespecified analyses were conducted to evaluate efficacy by PD-L1 status assessed by the VENTANA PD-L1 (SP263) Assay and by the PD-L1 IHC 22C3 pharmDxTM kit in all randomized patients with PD-L1 expression ≥ 1% tumor cells or ≥ 1% tumor-infiltrating immune cells by the VENTANA PD-L1 (SP142) Assay who do not have EGFR or ALK genomic tumor abberations (n=554). An OS improvement was observed with atezolizumab compared to chemotherapy in patients with high PD-L1 expression (PD-L1 ≥ 50% tumor cells) using the VENTANA PD-L1 (SP263) Assay (n=293; HR: 0.71 [95% CI: 0.50, 1.00], median OS 19.5 vs. 16.1 months) and in patients with high PD-L1 expression (Tumor Proportion Score (TPS) ≥ 50%) using the PD-L1 IHC 22C3 pharmDxTM Kit (n=260; HR: 0.60 [95% CI: 0.42, 0.86], median OS 20.2 vs. 11.0 months).

The study also evaluated Patient Reported Physical Function, Global Health Status/Health Related Quality of Life and Lung Related Symptoms using the EORTC QLQ-C30, EORTC QLQ-LC13, and SILC measures at the time of interim OS analysis. Patients who were randomized to Tecentriq (Arm A) on average reported sustained moderate improvement in physical functioning and no worsening in lung cancer-related symptoms (dyspnoea, cough, and chest pain) compared to patients randomized to chemotherapy (Arm B). Time to deterioration of these lung-related symptoms as measured by the SILC and EORTC QLQ-LC13 was similar in both treatment groups indicating that patients maintained low disease burden for a comparable duration of time.

DISETUJUI OLEH BPOM 8 MEI 2025 ID REG: EREG10043712400408-09

1L metastiatic non-squamous NSCLC

IMpower150

A phase III, open-label, randomized study, GO29436 (IMpower150), was conducted to evaluate the efficacy and safety of Tecentriq in combination with paclitaxel and carboplatin, with or without bevacizumab, in chemotherapy-naïve patients with metastatic non-squamous NSCLC. A total of 1202 patients were enrolled and were randomized in a 1:1:1 ratio to receive one of the treatment regimens described in Table 11. Randomization was stratified by sex, presence of liver metastases and PD-L1 tumor expression on tumor cells (TC) and tumor-infiltrating cells (IC).

Table 11 Intravenous treatment regimens in study IMpower150

Treatment regimen	Induction (Four or Six 21-day Cycles)	Maintenance (21-day Cycles)
A	Tecentriq[a] (1200 mg) + paclitaxel[b,c] (200 mg/m^2) + carboplatin[c] (AUC 6)	Tecentriq[a] (1200 mg)
B	Tecentriq[a] (1200 mg) + bevacizumab[d] (15 mg/kg) + paclitaxel[b,c] (200 mg/m^2) + carboplatin[c] (AUC 6)	Tecentriq[a] (1200 mg) + bevacizumab[d] (15 mg/kg)
C	Bevacizumab[d] (15 mg/kg) + paclitaxel[b,c] (200 mg/m^2) + carboplatin[c] (AUC 6)	Bevacizumab[d] (15 mg/kg)

[a]Tecentriq is administered until loss of clinical benefit as assessed by the investigator
[b]The paclitaxel starting dose for patients of Asian race/ethnicity was 175 mg/m^2 due to higher overall level of hematologic toxicities in patients from Asian countries compared with those from non-Asian countries
[c]Carboplatin and paclitaxel are administered until completion of 4 or 6 cycles, or progressive disease or unacceptable toxicity whichever occurs first
[d]Bevacizumab is administered until progressive disease or unacceptable toxicity

Patients were excluded if they had history of autoimmune disease; administration of a live, attenuated vaccine within 28 days prior to randomization; administration of systemic immunostimulatory agents within 4 weeks or systemic immunosuppressive medications within 2 weeks prior to randomization; active or untreated CNS metastases; clear tumor-infiltration into the thoracic great vessels or clear cavitation of pulmonary lesions, as seen on imaging. Tumor assessments were conducted every 6 weeks for the first 48 weeks following Cycle 1, Day 1 and then every 9 weeks thereafter.

The demographics and baseline disease characteristics of the study population were well balanced between the treatment arms. The median age was 63 years (range: 31 to 90), and 60% of patients were male. The majority of patients were white (82%). Approximately 10% of patients had known EGFR mutations, 4% had known ALK rearrangements, 14% had liver metastases at baseline, and most patients were current or previous smokers (80%). Baseline ECOG performance status was 0 (43%) or 1 (57%).

At the time of the final analysis for PFS, patients had a median follow-up time of 15.3 months. The ITT population, including patients with EGFR mutations or ALK rearrangements who should have been previously treated with tyrosine kinase inhibitors, demonstrated PFS improvement in Arm B as compared to Arm C (HR: 0.61 [95% CI: 0.52, 0.72] median PFS 8.3 vs. 6.8 months).

At the time of the interim OS analysis, patients had a median follow-up time of 19.7 months. The key results from this analysis are summarized in Table 12. Kaplan-Meier curves for OS in the ITT population are presented in Figure 7. Figure 8 summarizes the results of OS in the ITT and PD-L1 subgroups, demonstrating OS benefit with Tecentriq in all

DISETUJUI OLEH BPOM 8 MEI 2025 ID REG: EREG10043712400408-09

subgroups, including those with PD-L1 expression < 1% on TC and IC. Updated PFS results are also demonstrated in Figures 9 and 10.

Table 12 Summary of updated efficacy from IMpower150

Key efficacy endpoints	Arm B	Arm C
OS Interim Analysis	n=400	n=400
No. of deaths (%)	192 (48.0%)	230 (57.5%)
Median time to events (months)	19.8	14.9
95% CI	(17.4, 24.2)	(13.4, 17.1)
Stratified hazard ratio (95% CI)	0.76 (0.63, 0.93)	
p-value [1,2]	0.006	
6-month OS (%)	85	81
12-month OS (%)	68	61
Investigator-assessed PFS (RECIST v1.1)	n=400	n=400
No. of events (%)	291 (72.8%)	355 (88.8%)
Median duration of PFS (months)	8.4	6.8
95% CI	(8.0, 9.9)	(6.0, 7.0)
Stratified hazard ratio‡ (95% CI)	0.59 (0.50, 0.69)	
p-value [1,2]	< 0.0001	
12-month PFS (%)	38	20
Investigator-assessed Overall Best Response[3] (RECIST 1.1)	n=397	n=393
No. of responders (%)	224 (56.4%)	158 (40.2%)
95% CI	(51.4, 61.4)	(35.3, 45.2)
No. of complete response (%)	11 (2.8%)	3 (0.8%)
No. of partial response (%)	213 (53.7%)	155 (39.4%)
Investigator-assessed DOR (RECIST 1.1)	n=224	n=158
Median in months	11.5	6.0
95% CI	(8.9, 15.7)	(5.5, 6.9)

1. Based on the stratified log-rank test
2. For informational purposes; comparisons between Arm B and Arm C in the ITT population were not formally tested yet, as per the prespecified analysis hierarchy
3. Overall best response for complete response and partial response

‡ Stratified by sex, presence of liver metastases and PD-L1 tumor expression on TC and IC

PFS=progression-free survival; RECIST=response evaluation criteria in solid tumors v1.1; CI=confidence interval; ORR=objective response rate; DOR=duration of response; OS=overall survival

DISETUJUI OLEH BPOM 8 MEI 2025 ID REG: EREG10043712400408-09

Figure 7 Kaplan-Meier plot for overall survival in the ITT population (IMpower150)

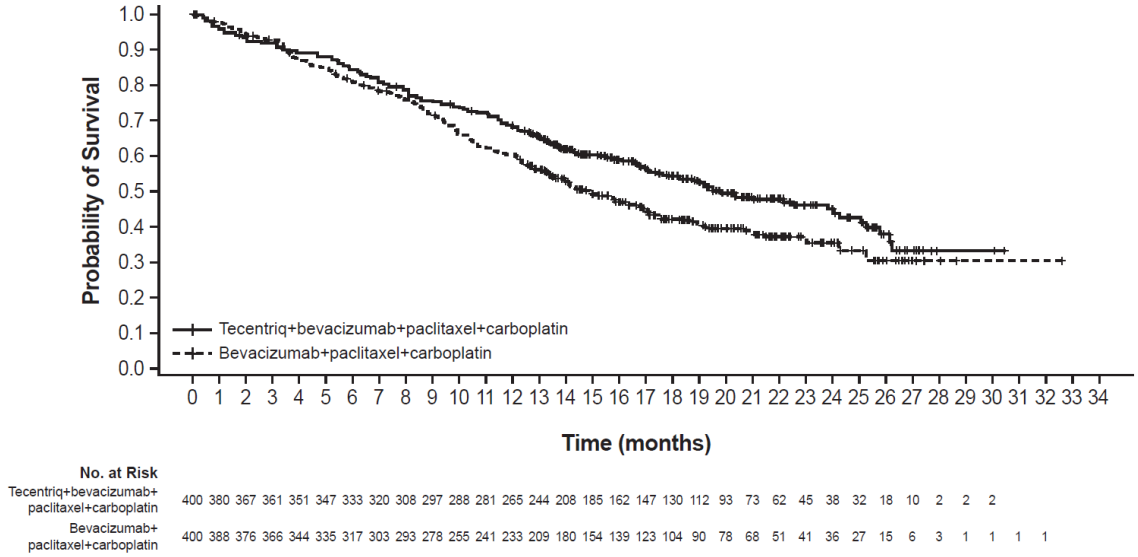
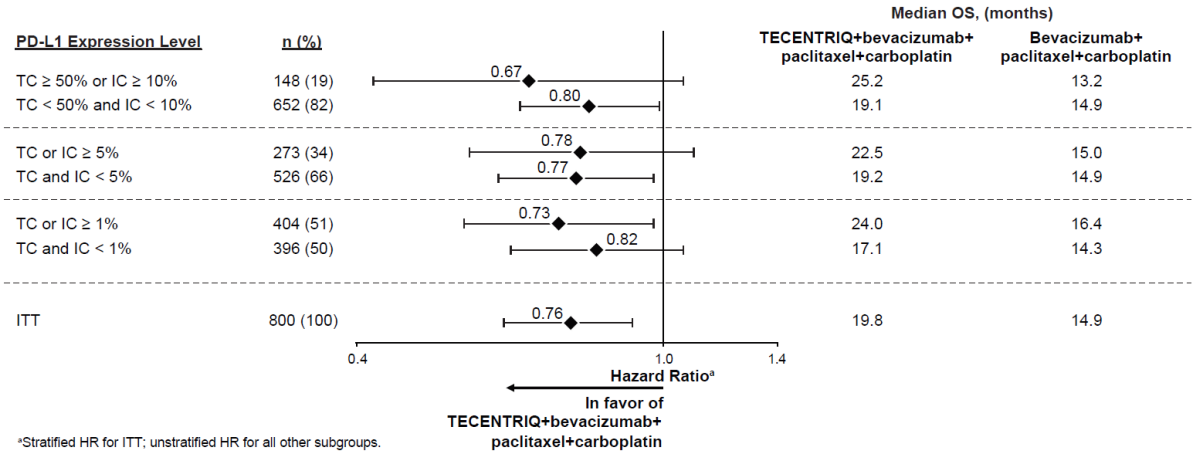


Figure 8 Forest plot of overall survival by PD-L1 expression in the ITT population (IMpower150)



DISETUJUI OLEH BPOM 8 MEI 2025 ID REG: EREG10043712400408-09

Figure 9 Kaplan-Meier plot for updated progression-free survival in the ITT population (IMpower150)

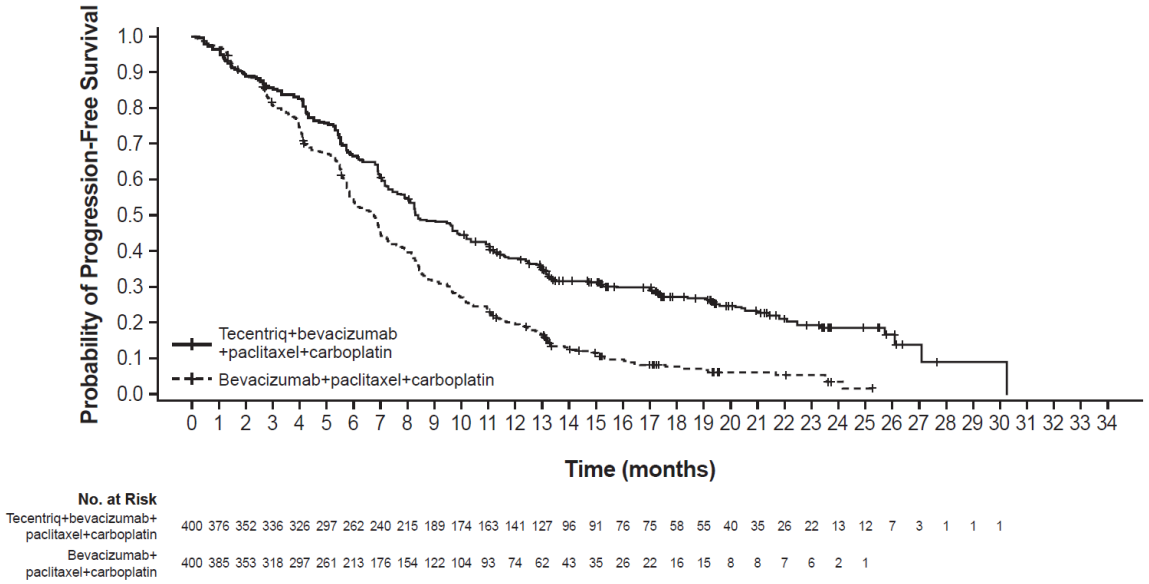
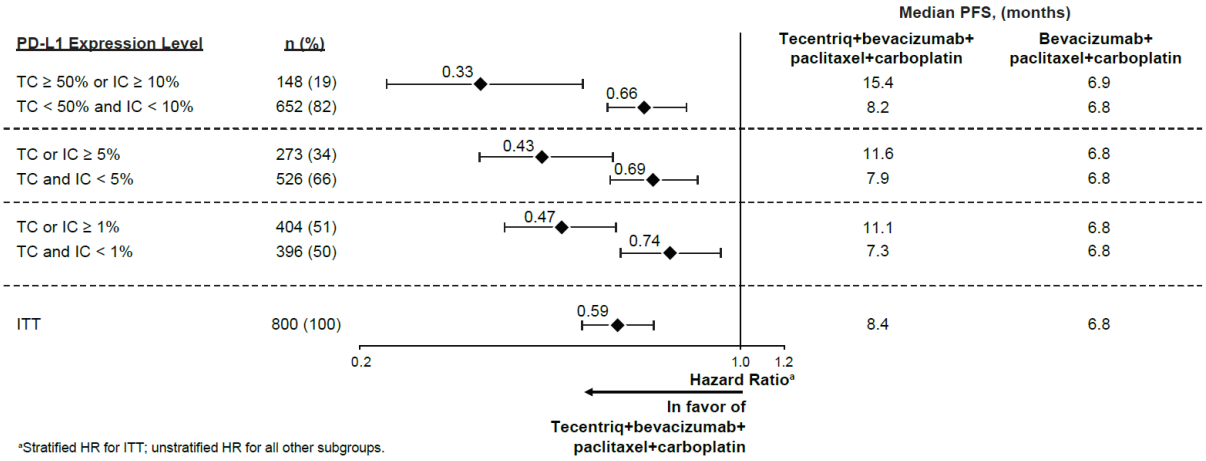


Figure 10 Forest plot of updated progression-free survival by PD-L1 expression in the ITT population (IMpower150)



Prespecified subgroup analyses from the interim OS analysis showed numerical OS improvements in the Tecentriq with bevacizumab, paclitaxel, carboplatin arm as compared to the bevacizumab, paclitaxel and carboplatin arm for patients with EGFR mutations or ALK rearrangements (HR: 0.54 [95% CI: 0.29, 1.03], median OS NE vs 17.5 months) and liver metastases (HR:0.52 [95% CI: 0.33, 0.82], median OS 13.3 vs. 9.4 months). Numerical PFS improvements were also shown in patients with EGFR mutations or ALK rearrangements (HR: 0.55 [95% CI 0.34, 0.90], median PFS 10 vs. 6.1 months) and liver metastases (HR: 0.41 [95%CI 0.26, 0.62], median PFS 8.2 vs. 5.4 months).

This study also evaluated Physical Function and Patient-Reported Treatment-Related Symptoms using the EORTC QLQ-C30 and EORTC QLQ-LC13 measures at the time of the final PFS analysis. On average, patients who received Tecentriq with bevacizumab, paclitaxel and carboplatin reported minimal treatment burden as indicated by minimal

DISETUJUI OLEH BPOM 8 MEI 2025 ID REG: EREG10043712400408-09

deterioration in both Physical Function and Patient-Reported Treatment-Related Symptom Scores (i.e. fatigue, constipation, diarrhoea, nausea/vomiting, hemoptysis, dysphagia, and sore mouth) while on treatment. Average patient-reported physical function and treatment-related symptom scores in both patients who received Tecentriq with bevacizumab, paclitaxel and carboplatin as well as patients who received bevacizumab in combination with paclitaxel and carboplatin, were comparable while on treatment.

1L ES – SCLC

IMpower133

A Phase I/III, randomized, multicenter, double-blind, placebo-controlled study, GO30081 (IMpower133), was conducted to evaluate the efficacy and safety of Tecentriq in combination with carboplatin and etoposide in patients with chemotherapy-naïve ES-SCLC. A total of 403 patients were randomized (1:1) to receive one of the treatment regimens described in Table 13. Randomization was stratified by sex, ECOG performance status, and presence of brain metastases.

This study excluded patients who had active or untreated CNS metastases; history of autoimmune disease; administration of live, attenuated vaccine within 4 weeks prior to randomization; administration of systemic immunosuppressive medications within 1 week prior to randomization. Tumor assessments were conducted every 6 weeks for the first 48 weeks following Cycle 1, Day 1 and then every 9 weeks thereafter. Patients treated beyond disease progression had tumor assessment conducted every 6 weeks until treatment discontinuation.

Table 13 Intravenous treatment regimen in study IMpower133

Treatment regimen	Induction (Four 21-day Cycles)	Maintenance (21-day Cycles)
A	Tecentriq (1200 mg)[a] + carboplatin (AUC 5)[b] + etoposide (100 mg/m^2)[b,c]	Tecentriq (1200 mg) [a]
B	placebo + carboplatin (AUC 5)[b] + etoposide (100 mg/m^2)[b,c]	placebo

[a]Tecentriq is administered until loss of clinical benefit as assessed by investigator
[b]Carboplatin and etoposide is administered until completion of 4 cycles, or progressive disease or unacceptable toxicity whichever occurs first
[c]Etoposide is administered on Day 1, 2 and 3 of each cycle

The demographic and baseline disease characteristics of the primary analysis population were well balanced between the treatment arms. The median age was 64 years (range: 26 to 90 years). The majority of patients were male (65%), white (80%), and 9% had brain metastases and most patients were current or previous smokers (97%). Baseline ECOG performance status was 0 (35%) or 1 (65%).

At the time of the primary analysis, patients had a median survival follow-up time of 13.9 months. The key results are summarized in Table 14. Kaplan-Meier curves for OS and PFS are presented in Figure 11 and 12.

DISETUJUI OLEH BPOM 8 MEI 2025 ID REG: EREG10043712400408-09

Table 14 Summary of efficacy from IMpower133

Key efficacy endpoints	**Arm A** (Tecentriq + carboplatin + etoposide)	**Arm B** (Placebo + carboplatin + etoposide)
Co-primary endpoints		
OS analysis	n=201	n=202
No. of deaths (%)	104 (51.7%)	134 (66.3%)
Median time to events (months)	12.3	10.3
95% CI	(10.8, 15.9)	(9.3, 11.3)
Stratified hazard ratio‡ (95% CI)	0.70 (0.54, 0.91)	
p-value	0.0069	
12-month OS (%)	51.7	38.2
Investigator-assessed PFS (RECIST v1.1)	n=201	n=202
No. of events (%)	171 (85.1%)	189 (93.6%)
Median duration of PFS (months)	5.2	4.3
95% CI	(4.4, 5.6)	(4.2, 4.5)
Stratified hazard ratio‡ (95% CI)	0.77 (0.62, 0.96)	
p-value	0.0170	
6-month PFS (%)	30.9	22.4
12-month PFS (%)	12.6	5.4
Secondary endpoints		
Investigator-assessed ORR (RECIST 1.1)	n=201	n=202
No. of responders (%)	121 (60.2%)	130 (64.4%)
95% CI	(53.1, 67.0)	(57.3, 71.0.)
No. of complete response (%)	5 (2.5%)	2 (1.0%)
No. of partial response (%)	116 (57.7%)	128 (63.4%)
Investigator-assessed DOR (RECIST 1.1)	n=121	n=130
Median in months	4.2	3.9
95% CI	(4.1, 4.5)	(3.1, 4.2)

PFS=progression-free survival; RECIST=response evaluation criteria in solid tumors v1.1; CI=confidence interval; ORR=objective response rate; DOR=duration of response; OS=overall survival

‡ Stratified by sex and ECOG performance status

DISETUJUI OLEH BPOM 8 MEI 2025 ID REG: EREG10043712400408-09

Figure 11 Kaplan-Meier plot of overall survival (IMpower133)

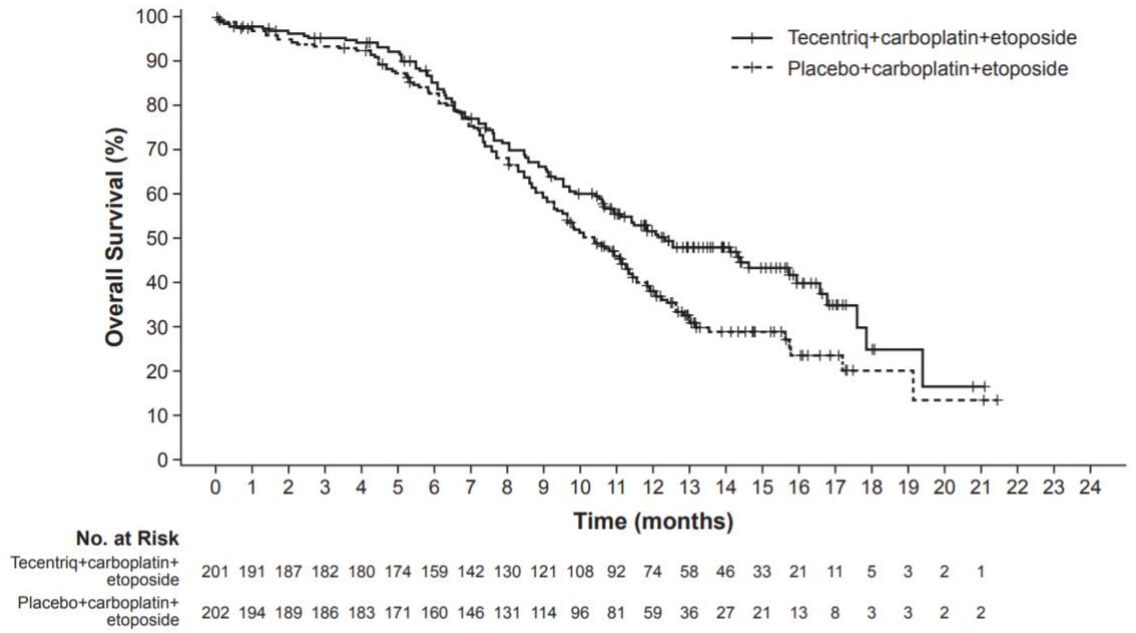
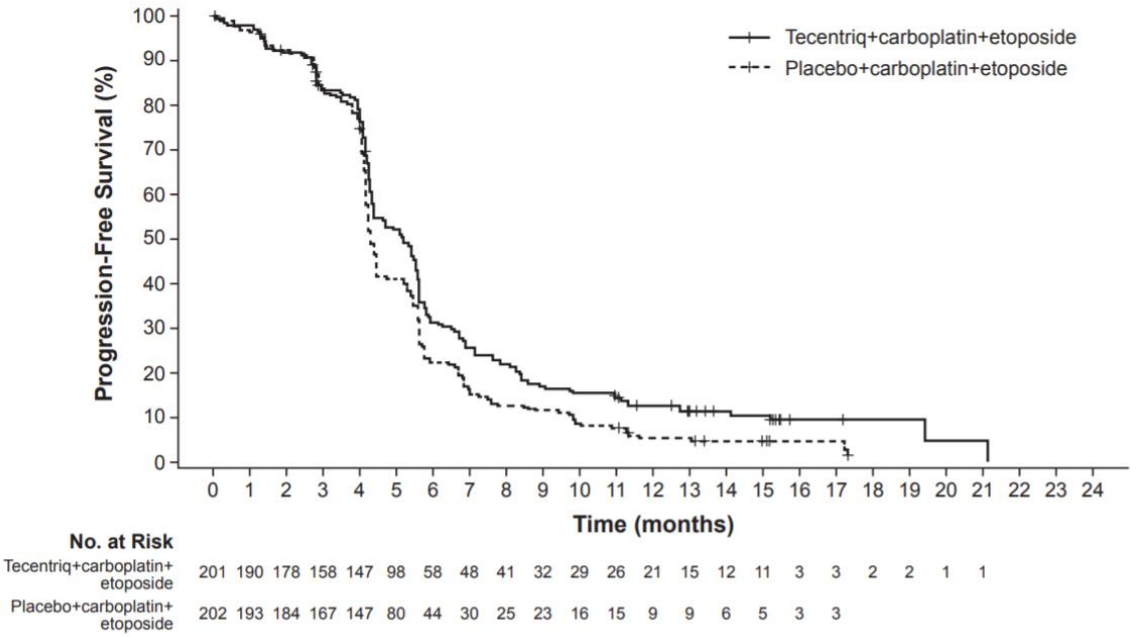


Figure 12 Kaplan-Meier plot of progression-free survival (IMpower133)



This study also included an exploratory analysis of average score changes from baseline in patient-reported symptoms, physical function, and health-related quality of life (measured using the EORTC QLC-C30 and QLC-LC13). On average, patients who received Tecentriq with carboplatin and etoposide reported early and notable improvements in lung cancer-related symptoms (e.g. coughing, chest pain, dyspnoea) and physical function. Changes in treatment-related symptoms (e.g. diarrhoea, nausea and vomiting, sore mouth, peripheral neuropathy) were comparable between arms throughout

DISETUJUI OLEH BPOM 8 MEI 2025 ID REG: EREG10043712400408-09

induction and most visits through Week 54. Overall, patients treated with Tecentriq, carboplatin and etoposide achieved more pronounced and enduring improvements in health-related quality of life (≥ 10-point score increases at most visits through Week 48) compared to patients treated with placebo, carboplatin and etoposide, who reported nominal improvements (< 10-point score increases) at most study treatment visits.

HCC

IMbrave150

A global phase III, randomized, multi-center, open-label study, YO40245 (IMbrave150), was conducted to evaluate the efficacy and safety of Tecentriq in combination with bevacizumab, in patients with locally advanced or metastatic and/or unresectable HCC, who have not received prior systemic treatment. A total of 501 patients were randomized (2:1) to receive either Tecentriq 1200 mg and 15 mg/kg of bevacizumab every 3 weeks administered via IV infusion, or sorafenib 400 mg orally twice per day. Randomization was stratified by geographic region (Asia excluding Japan vs. rest of world), macrovascular invasion and/or extrahepatic spread (presence vs. absence), baseline AFP (< 400 vs. ≥ 400 ng/mL) and ECOG performance status (0 vs. 1). Patients in both arms received treatment until loss of clinical benefit, or unacceptable toxicity. Patients could discontinue either Tecentriq or bevacizumab (e.g. due to adverse events) and continue on single-agent therapy until loss of clinical benefit or unacceptable toxicity associated with the single-agent.

The study enrolled adults who were Child-Pugh A, ECOG 0/1 and who had not received prior systemic treatment. Bleeding (including fatal events) is a known adverse reaction with bevacizumab and upper gastrointestinal bleeding is a common and life-threatening complication in patients with HCC. Hence, patients were required to be evaluated for the presence of varices within 6 months prior to treatment, and were excluded if they had variceal bleeding within 6 months prior to treatment, untreated or incompletely treated varices with bleeding or high risk of bleeding. Patients were also excluded if they had moderate or severe ascites; history of hepatic encephalopathy; a history of autoimmune disease; administration of a live, attenuated vaccine within 4 weeks prior to randomization; administration of systemic immunostimulatory agents within 4 weeks or systemic immunosuppressive medications within 2 weeks prior to randomization; untreated or corticosteroid-dependent brain metastases. Tumor assessments were performed every 6 weeks for the first 54 weeks following Cycle 1, Day 1, then every 9 weeks thereafter.

The demographic and baseline disease characteristics of the study population were well balanced between the treatment arms. The median age was 65 years (range: 26 to 88 years) and 83% were male. The majority of patients were Asian (57%) and white (35%). 40% were from Asia (excluding Japan), while 60% were from rest of world. Approximately 75% of patients presented with macrovascular invasion and/or extrahepatic spread and 37% had a baseline AFP ≥ 400 ng/mL. Baseline ECOG performance status was 0 (62%) or 1 (38%). The primary risk factors for the development of HCC were hepatitis B virus infection in 48% of patients, hepatitis C virus infection in 22% of patients, and non-viral disease in 31% of patients. HCC was categorized as Barcelona Clinic Liver Cancer (BCLC) stage C in 82% of patients, stage B in 16% of patients, and stage A in 3% of patients.

The co-primary efficacy endpoints were OS and IRF-assessed PFS according to RECIST v1.1. At the time of the primary analysis, patients had a median survival follow-up time of 8.6 months. The data demonstrated a statistically significant improvement in OS and PFS as assessed by IRF per RECIST v1.1 with Tecentriq + bevacizumab compared to

DISETUJUI OLEH BPOM 8 MEI 2025 ID REG: EREG10043712400408-09

sorafenib. A statistically significant improvement was also observed in confirmed objective response rate (ORR) by IRF per RECIST v1.1 and HCC modified RECIST (mRECIST). The key efficacy results from the primary analysis are summarized in Table 15.

A descriptive updated efficacy analysis was performed with a median survival follow-up time of 15.6 months. The key results from the updated analysis are summarized in Table 16. Kaplan-Meier curves for OS (updated analysis) and PFS (primary analysis) are presented in Figures 13 and 14, respectively.

Table 15 Summary of efficacy (IMbrave150 primary analysis)

Key efficacy endpoints	**Tecentriq + Bevacizumab**	**Sorafenib**
OS	n=336	n=165
No. of deaths (%)	96 (28.6%)	65 (39.4%)
Median time to event (months)	NE	13.2
95% CI	(NE, NE)	(10.4, NE)
Stratified hazard ratio‡ (95% CI)	0.58 (0.42, 0.79)	
p-value[1]	0.0006	
6-month OS (%)	84.8%	72.3%

	RECIST v1.1		**HCC mRECIST**	
	Tecentriq + bevacizumab	Sorafenib	Tecentriq + bevacizumab	Sorafenib
IRF-assessed PFS	n=336	n=165	n=336	n=165
No. of events (%)	197 (58.6%)	109 (66.1%)	199 (59.2%)	111 (67.3%)
Median duration of PFS (months)	6.8	4.3	6.8	4.2
95% CI	(5.8, 8.3)	(4.0, 5.6)	(5.7, 7.7)	(4.0, 5.5)
Stratified hazard ratio‡ (95% CI)	0.59 (0.47, 0.76)		0.59 (0.46, 0.74)	
p-value[1]	< 0.0001		N/A	
6-month PFS	54.5%	37.2%	54.3%	36.4%
IRF-assessed ORR	n=326	n=159	n=325	n=158
No. of confirmed responders (%)	89 (27.3%)	19 (11.9%)	108 (33.2%)	21 (13.3%)
95% CI	(22.5, 32.5)	(7.4, 18.0)	(28.1, 38.6)	(8.4, 19.6)
p-value[2]	< 0.0001		< 0.0001	
No. of complete responses (%)	18 (5.5%)	0	33 (10.2%)	3 (1.9%)
No. of partial responses (%)	71 (21.8%)	19 (11.9%)	75 (23.1%)	18 (11.4%)
No. of stable disease (%)	151 (46.3%)	69 (43.4%)	127 (39.1%)	66 (41.8%)
IRF-assessed DOR	n=89	n=19	n=108	n=21
Median in months	NE	6.3	NE	6.3
95% CI	(NE, NE)	(4.7, NE)	(NE, NE)	(4.9, NE)
6-month DOR (%)	87.6%	59.1%	82.3%	62.5%

‡ Stratified by geographic region (Asia excluding Japan vs. rest of world), macrovascular invasion and/or extrahepatic spread (presence vs. absence), and baseline AFP (< 400 vs. ≥ 400 ng/mL)

[1] Based on two-sided stratified log-rank test

[2] Based on two-sided Cochran-Mantel-Haenszel test

PFS=progression-free survival; RECIST=response evaluation criteria in solid tumors v1.1; HCC mRECIST=modified RECIST assessment for hepatocellular carcinoma; CI=confidence interval; ORR=objective response rate; DOR=duration of response; OS=overall survival; NE=not estimable; N/A=not applicable

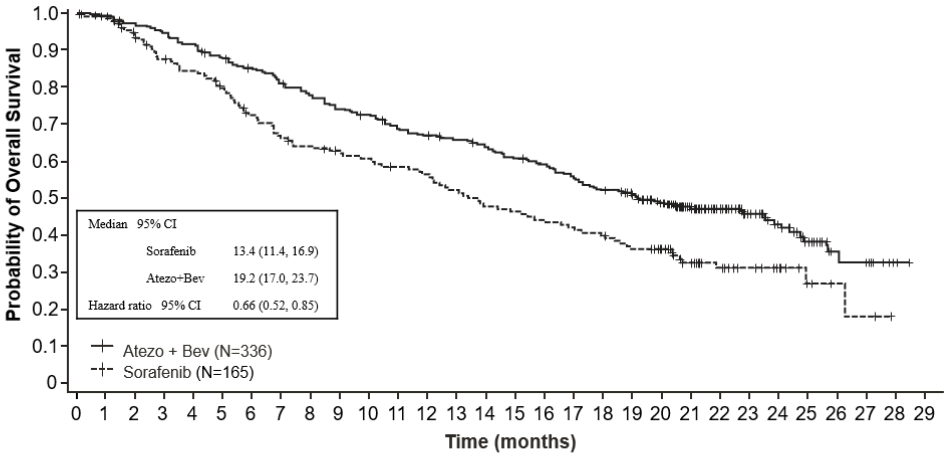
DISETUJUI OLEH BPOM 8 MEI 2025 ID REG: EREG10043712400408-09

Table 16 Summary of efficacy (IMbrave150 updated analysis)

Key efficacy endpoints	Atezolizumab + Bevacizumab	Sorafenib
OS	n=336	n=165
No. of deaths (%)	180 (53.6%)	100 (60.6%)
Median time to event (months)	19.2	13.4
95% CI	(17.0, 23.7)	(11.4, 16.9)
Stratified hazard ratio‡ (95% CI)	0.66 (0.52, 0.85)	
IRF-assessed ORR, RECIST 1.1	n=326	n=159
No. of confirmed responders (%)*	97 (29.8%)	18 (11.3%)
95% CI	(24.8, 35.0)	(6.9, 17.3)
IRF-assessed DOR, RECIST 1.1	n=97	n=18
Median in months	18.1	14.9
95% CI	(14.6, NE)	(4.9, 17.0)

‡ Stratified by geographic region (Asia excluding Japan vs. rest of world), macrovascular invasion and/or extrahepatic spread (presence vs. absence), and baseline AFP (< 400 vs. ≥ 400 ng/mL)
* No. of complete responses (%): 25 (7.7%) in the atezolizumab + bevacizumab arm and 1 (0.6%) in the sorafenib arm
PFS=progression-free survival; RECIST=response evaluation criteria in solid tumors v1.1; CI=confidence interval; ORR=objective response rate; DOR=duration of response; OS=overall survival; NE=not estimable

Figure 13 Kaplan-Meier curve for overall survival (IMbrave150 updated analysis)



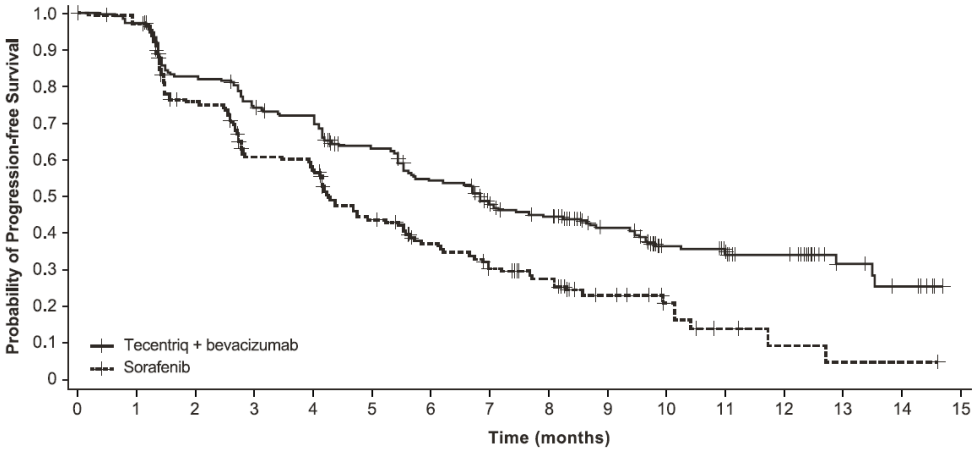
No. of Patients at Risk

Atezo + Bev	336	329	320	312	302	288	276	263	252	240	233	221	214	209	202	192	186	175	164	156	134	105	80	57	42	24	12	11	2	NE
Sorafenib	165	158	144	133	128	119	106	96	92	88	85	81	78	72	66	64	61	58	55	49	44	32	24	18	12	7	3	2	NE	NE

Hazard ratio is from stratified analysis. Stratification factors include geographic region (Asia excluding Japan vs. rest of world), macrovascular invasion and/or extrahepatic spread (presence vs absence) and AFP (<400 vs >=400 ng/ml) at screening per IxRS.

DISETUJUI OLEH BPOM 8 MEI 2025 ID REG: EREG10043712400408-09

Figure 14 Kaplan-Meier plot for progression-free survival per RECIST v1.1 (IMbrave150 primary analysis)



No. of Patients at Risk															
Tecentriq + bevacizumab	336	322	270	243	232	201	169	137	120	74	50	46	34	11	7	NE
Sorafenib	165	148	109	84	80	57	44	34	27	15	9	4	2	1	1	NE

The study evaluated patient-reported outcomes using the EORTC QLQ-C30 and EORTC QLQ-HCC18 questionnaires. Time to deterioration (TTD) of patient-reported physical functioning, role functioning, and global health status/quality of life (GHS/QoL) on the EORTC QLQ-C30 were prespecified secondary endpoints. TTD was defined as the time from randomization to the first deterioration (decrease from baseline of ≥ 10 points) maintained for two consecutive assessments, or one assessment followed by death from any cause within 3 weeks. Compared with sorafenib, treatment with Tecentriq and bevacizumab delayed deterioration of patient-reported physical functioning (median TTD: 13.1 vs. 4.9 months; HR 0.53, 95% CI 0.39, 0.73), role functioning (median TTD: 9.1 vs. 3.6 months; HR 0.62, 95% CI 0.46, 0.84), and GHS/QoL (median TTD: 11.2 vs. 3.6 months; HR 0.63, 95% CI 0.46, 0.85). In prespecified exploratory analyses, compared with sorafenib, treatment with Tecentriq and bevacizumab also delayed deterioration of patient-reported symptoms (i.e. appetite loss, diarrhoea, fatigue, pain, and jaundice) on the EORTC QLQ-C30 and EORTC QLQ-HCC18.

GO30140

A global, open-label, multi-center, multi-arm Phase Ib study (GO30140) was also conducted in patients with solid tumors. Arm F of the study used a randomized design to evaluate the safety and efficacy of Tecentriq administered in combination with bevacizumab versus Tecentriq monotherapy in patients with advanced or metastatic and/or unresectable HCC who had not received prior systemic treatment. The primary efficacy endpoint was PFS assessed by IRF according to RECIST v1.1. A total of 119 patients were randomized 1:1 to receive either Tecentriq (1200 mg) and bevacizumab (15 mg/kg) by IV infusion every 3 weeks or Tecentriq (1200 mg) every 3 weeks. At the time of the primary analysis, the median survival follow-up was 6.6 months. The combination of Tecentriq with bevacizumab showed statistically significant PFS benefit compared to Tecentriq monotherapy (HR of 0.55, 80% CI: 0.40, 0.74, p-value=0.0108)

DISETUJUI OLEH BPOM 8 MEI 2025 ID REG: EREG10043712400408-09

with a median PFS of 5.6 months in patients treated with Tecentriq and bevacizumab, vs. 3.4 months in patients treated with Tecentriq monotherapy.

3.1.3 Immunogenicity

As with all therapeutic proteins, there is the potential for immune response to atezolizumab. Across multiple phase III studies, 13.1% to 36.4% of patients developed treatment-emergent anti-drug antibodies (ADAs) and 4.3% to 19.7% of patients developed neutralizing antibodies (NAbs). ADA and Nab status appeared to have no clinically relevant impact on atezolizumab pharmacokinetics, efficacy or safety.

Immunogenicity assay results are highly dependent on several factors including assay sensitivity and specificity, assay methodology, sample handling, timing of sample collection, concomitant medications and underlying disease. For these reasons, comparison of incidence of antibodies to Tecentriq with the incidence of antibodies to other products may be misleading.

3.2 PHARMACOKINETIC PROPERTIES

The pharmacokinetics of atezolizumab have been characterized in patients in multiple clinical trials at doses 0.01 mg/kg to 20 mg/kg and 1200 mg every 3 weeks, as well as 840 mg every 2 weeks. Exposure to atezolizumab increased dose proportionally over the dose range 1 mg/kg to 20 mg/kg. A population analysis that included 472 patients described atezolizumab pharmacokinetics for the dose range: 1-20 mg/kg with a linear two-compartment disposition model with first-order elimination. Based on pharmacokinetic modeling, the overall exposure of atezolizumab administered at doses of 840 mg every 2 weeks, 1200 mg every 3 weeks, and 1680 mg every 4 weeks are comparable. A population pharmacokinetic analysis suggests that steady-state is obtained after 6 to 9 weeks after multiple doses. The maximum systemic accumulation ratio across dosing regimens is 3.3.

Based on an analysis of exposure, safety and efficacy data, the following factors have no clinically relevant effect: age (21-89 years), body weight, gender, positive ADA status, albumin levels, tumor burden, region or ethnicity, renal impairment, mild hepatic impairment, level of PD-L1 expression, or ECOG status.

3.2.1 Absorption

Tecentriq is administered as an IV infusion. There have been no studies performed with other routes of administration.

3.2.2 Distribution

A population pharmacokinetic analysis indicates that central compartment volume of distribution (V_1) is 3.28 L and volume at steady-state ($Vs._s$) is 6.91 L in the typical patient.

3.2.3 Metabolism

The metabolism of Tecentriq has not been directly studied. Antibodies are cleared principally by catabolism.

3.2.4 Elimination

A population pharmacokinetic analysis indicates that the clearance of atezolizumab is 0.200 L/day and the typical terminal elimination half-life ($t_{1/2}$) is 27 days.

DISETUJUI OLEH BPOM 8 MEI 2025 ID REG: EREG10043712400408-09

3.2.5 Pharmacokinetics in Special Populations

Pediatric population

No studies have been conducted to investigate the pharmacokinetics of Tecentriq in children.

Geriatric population

No dedicated studies of Tecentriq have been conducted in geriatric patients. The effect of age on the pharmacokinetics of atezolizumab was assessed in a population pharmacokinetic analysis. Age was not identified as a significant covariate influencing atezolizumab pharmacokinetics based on patients of age range of 21-89 years (n=472), and median of 62 years of age. No clinically important difference was observed in the pharmacokinetics of atezolizumab among patients < 65 years (n=274), patients between 65–75 years (n=152) and patients > 75 years (n=46) (see section *2.2.1 Special Dosage Instructions*).

Renal impairment

No dedicated studies of Tecentriq have been conducted in patients with renal impairment. In the population pharmacokinetic analysis, no clinically important differences in the clearance of atezolizumab were found in patients with mild (eGFR 60 to 89 mL/min/1.73 m^2; n=208) or moderate (eGFR 30 to 59 mL/min/1.73 m^2; n=116) renal impairment compared to patients with normal (eGFR greater than or equal to 90 mL/min/1.73 m^2; n=140) renal function. Only a few patients had severe renal impairment (eGFR 15 to 29 mL/min/1.73 m^2; n=8) (see section *2.2.1 Special Dosage Instructions*).

Hepatic impairment

No dedicated studies of Tecentriq have been conducted in patients with hepatic impairment. In the population pharmacokinetic analysis, there were no clinically important differences in the clearance of atezolizumab between patients with mild hepatic impairment (bilirubin ≤ ULN and AST > ULN or bilirubin > 1.0 to 1.5 × ULN and any AST) or moderate hepatic impairment (bilirubin > 1.5 to 3x ULN and any AST). No data are available in patients with severe (bilirubin > 3.0 × ULN and any AST) hepatic impairment. Hepatic impairment was defined by the National Cancer Institute (NCI) criteria of hepatic dysfunction (see section *2.2.1 Special Dosage Instructions*).

3.3 NONCLINICAL SAFETY

3.3.1 Carcinogenicity

No carcinogenicity studies have been conducted with Tecentriq.

3.3.2 Genotoxicity

No mutagenicity studies have been conducted with Tecentriq.

3.3.3 Impairment of Fertility

No fertility studies have been conducted with Tecentriq; however, assessment of the cynomolgus monkey male and female reproductive organs was included in the chronic toxicity study. Tecentriq had an effect on menstrual cycles in all female monkeys in the 50 mg/kg dose group characterized by an irregular cycle pattern during the dosing phase and correlated with the lack of fresh corpora lutea in the ovaries at the terminal necropsy; this effect was reversible during the dose-free recovery period. There was no effect on the male reproductive organs.

DISETUJUI OLEH BPOM 8 MEI 2025 ID REG: EREG10043712400408-09

3.3.4 Reproductive Toxicity

No reproductive or teratogenicity studies in animals have been conducted with Tecentriq. The PD-L1/PD-1 signaling pathway is well established as essential in maternal/fetal tolerance and embryo-fetal survival during gestation. Administration of Tecentriq is expected to have an adverse effect on pregnancy and poses a risk to the human fetus, including embryo lethality.

3.3.5 Other

Not applicable.

4. PHARMACEUTICAL PARTICULARS

4.1 STORAGE

Vials

Store at 2°C-8°C.
Tecentriq should be protected from light.
Do not freeze. Do not shake.
This medicine should not be used after the expiry date (EXP) shown on the pack.
The diluted solution for infusion should be used immediately. If the solution is not used immediately, it can be stored for up to 30 days at 2°C-8°C, or 24 hours at ambient temperature (≤ 25°C), if prepared under aseptic conditions.

4.2 SPECIAL INSTRUCTIONS FOR USE, HANDLING AND DISPOSAL

Instructions for dilution

Tecentriq should be prepared by a health care professional using aseptic technique. Use sterile needle and syringe to prepare Tecentriq. Withdraw the required volume of Tecentriq liquid concentrate from the vial and dilute to the required administration volume with 0.9% sodium chloride solution. Dilute with 0.9% sodium chloride injection only. After dilution, the final concentration of the diluted solution should be between 3.2 and 16.8 mg/mL.

This medicinal product must not be mixed with other medicinal products.

No preservative is used in Tecentriq therefore each vial is for single-use only. Discard any unused portion.

Incompatibilities

No incompatibilities have been observed between Tecentriq and IV bags with product-contacting surfaces of polyvinyl chloride (PVC), polyolefin bags, polyethylene (PE) or polypropylene (PP). In addition, no incompatibilities have been observed with in-line filter membranes composed of polyethersulfone or polysulfone, and infusion sets and other infusion aids composed of PVC, PE, polybutadiene, or polyetherurethane.

Disposal of unused/expired medicines

The release of pharmaceuticals in the environment should be minimized. Medicines should not be disposed of via wastewater and disposal through household waste should be avoided. Use established “collection systems”, if available in your location.

4.3 PACKS

Tecentriq 1200 mg/20 mL

Box, 1 vial @ 20 mL Reg. No.: DKI2157509949A1

DISETUJUI OLEH BPOM 8 MEI 2025 ID REG: EREG10043712400408-09

Tecentriq 840 mg/14 mL

Box, 1 vial @ 14 mL Reg. No.: DKI2157509949B1

Medicine: keep out of reach and sight of children
On Medical Prescription Only
HARUS DENGAN RESEP DOKTER

Pada proses pembuatannya bersinggungan dengan bahan bersumber babi.

Tecentriq 1200 mg/20 mL & Tecentriq 840 mg/14 mL

Made by:

F. Hoffman-La Roche Ltd., Kaiseraugst, Switzerland

for F. Hoffman-La Roche Ltd., Basel, Switzerland

Imported by:

PT Menarini Indria Laboratories, Bekasi, Indonesia

Distributed by:

PT Roche Indonesia, Jakarta, Indonesia

This PI draft has been reviewed and approved by Pramelita and Lissa on 19 November 2024

DISETUJUI OLEH BPOM 8 MEI 2025 ID REG: EREG10043712400408-09

INFORMASI PRODUK UNTUK PASIEN
TECENTRIQ®
Atezolizumab
Konsentrat untuk larutan infus
1200 mg/20 mL
840 mg/14 mL

Bacalah brosur ini dengan saksama sebelum Anda mulai menggunakan obat ini karena brosur ini berisi informasi yang penting bagi Anda.

- Simpanlah brosur ini. Anda mungkin perlu membacanya kembali.
- Jika Anda memiliki pertanyaan lebih lanjut, tanyakan pada dokter, apoteker atau perawat Anda.
- Obat ini diresepkan hanya untuk Anda. Jangan memberikannya kepada orang lain. Obat ini dapat membahayakan mereka, walaupun tanda-tanda penyakit mereka serupa dengan penyakit Anda.
- Jika Anda mengalami efek samping, bicarakanlah dengan dokter, apoteker atau perawat Anda. Hal ini termasuk efek samping yang mungkin terjadi di luar dari apa yang tercantum pada brosur ini. Lihat bagian 4.

Apa yang terdapat dalam brosur ini

1. Apa itu TECENTRIQ® dan kegunaannya

Apa itu TECENTRIQ®

TECENTRIQ® adalah obat antikanker yang mengandung zat aktif ‘atezolizumab’. Zat tersebut adalah sejenis protein yang termasuk dalam kelompok obat yang disebut ‘antibodi monoklonal’. Antibodi monoklonal adalah sejenis protein yang dirancang untuk mengenali dan menempel pada zat target spesifik dalam tubuh.

Apa kegunaan TECENTRIQ®

TECENTRIQ® digunakan untuk mengobati orang dewasa dengan:

- Kanker pada kandung kemih dan sistem kemih, yang disebut ‘karsinoma urotelial’. TECENTRIQ® digunakan pada kanker kandung kemih setelah mendapatkan obat kemoterapi berbasis platinum bila terdapat:
  - Penyebaran ke bagian tubuh lain
  - Muncul kembali setelah pengobatan sebelumnya
- Kanker pada paru-paru, yang disebut kanker paru karsinoma bukan sel kecil (KPKBSK) /*non-small cell lung cancer* (NSCLC). Obat ini digunakan pada kanker ini setelah mendapatkan obat kemoterapi berbasis platinum bila terdapat:
  - Penyebaran ke bagian tubuh lain

DISETUJUI OLEH BPOM 8 MEI 2025 ID REG: EREG10043712400408-09

  - Muncul kembali setelah pengobatan sebelumnya

  Jika Anda belum pernah mendapatkan obat antikanker sebelumnya untuk pengobatan kanker paru-paru tingkat lanjut Anda, TECENTRIQ® akan digunakan jika dokter Anda sudah melakukan pengujian pada kanker Anda dan menemukan banyak protein spesifik yang disebut ligan kematian sel terprogram/*programmed-death ligand 1 (PD-L1).*

  Jika Anda belum pernah mendapatkan obat kemoterapi sebelumnya untuk pengobatan kanker paru-paru tingkat lanjut Anda, TECENTRIQ® akan diberikan kepada Anda dikombinasikan dengan obat lainnya yaitu bevacizumab dan kemoterapi (*carboplatin* dan *paclitaxel*). Penting untuk membaca informasi produk kombinasi tersebut.
- Kanker paru karsinoma bukan sel kecil (KPKBSK) stadium II-IIIA tahap awal. TECENTRIQ® diberikan setelah operasi pengangkatan tumor dan setelah kemoterapi.
- Kanker pada paru-paru, yang disebut kanker paru karsinoma sel kecil (KPKSK)/*small cell lung cancer* (SCLC). Tecentriq dapat digunakan apabila:
  - Kanker paru sudah menyebar ke bagian tubuh lainnya (perluasan)
  - Anda belum pernah menerima kemoterapi untuk kanker paru sel kecil yang sudah meluas

  Untuk mengobati kanker paru sel kecil yang sudah meluas ini, TECENTRIQ® akan diberikan kepada Anda dikombinasikan dengan *carboplatin* dan *etoposide*.
- Kanker pada hati yang disebut tipe 'karsinoma hepatoselular'. TECENTRIQ® digunakan bersama dengan obat antikanker lain yang disebut bevacizumab (Avastin). TECENTRIQ® diberikan apabila:
  - kanker hati tipe karsinoma hepatoselular tersebut tidak dapat dioperasi
  - Anda belum pernah mendapatkan pengobatan sebelumnya

Penting untuk membaca informasi produk kombinasi tersebut.

Bagaimana TECENTRIQ® bekerja

TECENTRIQ® bekerja dengan menempel pada protein spesifik dalam tubuh Anda yang disebut 'PD-L1'. Protein ini menekan sistem kekebalan tubuh (pertahanan), sehingga melindungi sel-sel kanker dari penyerangan oleh sel-sel kekebalan tubuh. Dengan menempel pada protein ini, TECENTRIQ® membantu sistem kekebalan tubuh Anda untuk melawan kanker.

2. Apa yang perlu Anda ketahui sebelum Anda diberikan TECENTRIQ®

Anda tidak boleh menggunakan TECENTRIQ® bila:

- Anda alergi pada atezolizumab atau bahan-bahan lain dari obat ini (tercantum pada bagian 6).

Bila Anda tidak yakin, diskusikan dengan dokter, apoteker atau perawat Anda sebelum Anda menggunakan TECENTRIQ®.

Peringatan dan perhatian

Diskusikan dengan dokter, apoteker atau perawat Anda sebelum Anda menggunakan TECENTRIQ® bila:

- Anda memiliki penyakit autoimun, yaitu kondisi dimana sistem kekebalan tubuh menyerang sel-sel sendiri
- Anda pernah mengalami peradangan pada paru-paru – yang disebut 'pneumonitis'
- Menderita kanker yang menyebar ke otak

DISETUJUI OLEH BPOM 8 MEI 2025 ID REG: EREG10043712400408-09

- Menderita atau pernah menderita infeksi virus kronis pada hati, termasuk hepatitis B atau hepatitis C
- Menderita infeksi HIV atau AIDS
- Mendapat vaksin dalam 28 hari sebelumnya
- Mendapat obat yang memengaruhi sistem kekebalan tubuh 2 minggu sebelumnya
- Mengalami efek samping serius dikarenakan terapi antibodi lain yang membantu sistem kekebalan tubuh melawan kanker

Bila salah satu hal di atas terjadi pada Anda (atau Anda tidak yakin), tanyakan pada dokter, apoteker atau perawat Anda sebelum Anda menggunakan TECENTRIQ®.

TECENTRIQ® dapat menyebabkan beberapa efek samping yang harus Anda sampaikan pada dokter, apoteker atau perawat Anda dengan segera. Hal tersebut dapat terjadi berminggu-minggu atau bahkan berbulan-bulan setelah pemberian dosis terakhir Anda. Segera sampaikan pada dokter, apoteker atau perawat Anda bila Anda menemukan gejala manapun di bawah ini:

- Peradangan pada paru-paru (pneumonitis): gejala dapat mencakup batuk yang baru atau pemburukan batuk yang lama, sesak napas, dan nyeri dada
- Peradangan pada hati (hepatitis): gejala dapat mencakup kulit atau mata yang menguning, mual, muntah, perdarahan atau memar, urine berwarna gelap, dan nyeri perut
- Peradangan pada usus (kolitis): gejala dapat mencakup diare (buang air besar berair, encer, atau lembek), darah dalam feses, dan nyeri perut
- Peradangan pada kelenjar tiroid, adrenal atau pituitari (hipotiroidisme, hipertiroidisme, insufisiensi adrenal atau hipofisitis): gejala dapat mencakup kelelahan, penurunan berat badan, peningkatan berat badan, perubahan suasana hati, rambut rontok, konstipasi, pusing, sakit kepala, sering merasa haus, sering buang air kecil, perubahan pada pandangan mata
- Diabetes melitus tipe 1, termasuk asam dalam darah yang terjadi karena diabetes (ketoasidosis diabetes): gejala dapat mencakup perasaan lebih lapar atau haus dari biasanya, keinginan buang air kecil lebih sering, penurunan berat badan, dan merasa lelah
- Peradangan pada otak (ensefalitis) atau peradangan pada selaput di sekitar saraf tulang belakang dan otak (meningitis): gejala dapat mencakup kaku leher, sakit kepala, demam, menggigil, muntah, mata yang sensitif terhadap cahaya, kebingungan, dan mengantuk
- Peradangan atau masalah pada saraf (neuropati): gejala dapat mencakup kelemahan otot dan kebas, rasa kesemutan pada tangan dan kaki
- Peradangan pada pankreas (pankreatitis): gejala dapat mencakup nyeri perut, mual, dan muntah
- Peradangan pada otot jantung (miokarditis): gejala dapat mencakup napas pendek, penurunan toleransi olahraga, rasa lelah, nyeri dada, pembengkakan pada pergelangan kaki dan kaki, detak jantung yang tidak beraturan, pingsan
- Peradangan pada ginjal (nefritis): gejala dapat mencakup perubahan pada warna dan jumlah urine, nyeri pada panggul, dan pembengkakan pada tubuh yang dapat menyebabkan gagal ginjal
- Peradangan pada otot (miositis): gejala dapat mencakup kelemahan otot, nyeri otot, ruam kulit pada dermatomiositis, peningkatan kreatinin-kinase serum
- Reaksi berat yang terkait dengan infus (kejadian yang berlangsung selama atau dalam satu hari saat menerima infus) dapat mencakup demam, menggigil, napas tersengal-sengal, atau kulit memerah (*flushing*)
- Erupsi obat berat/*Severe Cutaneous Adverse Reactions* (SCARs) yang diperantarai secara imunologis

DISETUJUI OLEH BPOM 8 MEI 2025 ID REG: EREG10043712400408-09

- Gangguan pada selaput pembungkus jantung (perikardium): gejala dapat mencakup nyeri atau rasa penuh pada dada, detak jantung tidak teratur, merasa lelah, kesulitan bernafas atau berbicara, atau nafas pendek.
- Gangguan sistem imun *haemophagocytic lymphohistiocytosis* (HLH): gejala dapat mencakup ruam kulit, warna kuning pada kulit dan mata Anda, batuk, kesulitan bernapas, sakit perut, muntah dan diare, sakit kepala, kesulitan berjalan, gangguan penglihatan dan lemah.
- Kelumpuhan pada otot-otot wajah yang diaktifkan oleh saraf wajah (*facial paresis*): gejala dapat mencakup gangguan saraf wajah pada satu sisi, seperti sudut mulut dan mata yang terkulai, kesulitan mengernyit, kesulitan menutup kelopak mata, pengurangan pembentukan air mata, peka terhadap kebisingan, produksi air liur berkurang dan gangguan persepsi rasa.
- Peradangan pada satu bagian saraf tulang belakang (myelitis): gejala dapat mencakup rasa nyeri, kebas atau mati rasa, lemah di tungkai atau lengan, serta gangguan buang air kecil dan buang air besar.
- Mulut kering (*dry mouth*): gejala dapat mencakup bibir kering, rasa sakit atau terbakar pada mulut, bau mulut, sariawan, kerusakan gigi dan gusi, kesulitan berbicara, makan dan menelan.

Bila Anda menemukan gejala manapun yang tertera di atas, segera sampaikan pada dokter, apoteker atau perawat Anda.

Jangan mencoba mengobati diri Anda sendiri dengan obat lainnya. Dokter Anda dapat:

- Memberikan obat lain untuk mencegah komplikasi dan mengurangi gejala
- Menunda pemberian dosis TECENTRIQ® Anda selanjutnya
- Menghentikan pengobatan Anda dengan TECENTRIQ®

Uji dan pemeriksaan

Sebelum pengobatan Anda, dokter Anda akan memeriksa kesehatan Anda secara umum. Pemeriksaan darah juga akan dilakukan selama menjalani pengobatan.

Anak-anak dan remaja

Obat ini tidak boleh diberikan pada anak atau yang berusia di bawah 18 tahun. Hal ini dikarenakan efek dari TECENTRIQ® pada kelompok usia ini belum diketahui.

Obat-obatan lain dan TECENTRIQ®

Sampaikan pada dokter, apoteker atau perawat Anda bila baru-baru ini atau saat ini Anda mengonsumsi atau mungkin menerima obat-obatan lainnya.

Hal ini mencakup obat-obatan yang didapatkan tanpa resep, termasuk obat-obatan herbal.

Penggunaan obat steroid atau obat yang menekan sistem kekebalan tubuh lainnya sebelum menggunakan TECENTRIQ® tidak diperbolehkan.

Kehamilan dan kontrasepsi

Sebelum memulai pengobatan ini:

- Sampaikan pada dokter Anda bila Anda sedang hamil, berpikir Anda mungkin hamil, atau berencana untuk hamil.
- Jangan gunakan TECENTRIQ® bila Anda sedang hamil kecuali dokter Anda sudah meminta Anda untuk menggunakannya. Hal ini dikarenakan efek TECENTRIQ® pada perempuan hamil belum diketahui – terdapat kemungkinan obat ini dapat membahayakan janin Anda.

DISETUJUI OLEH BPOM 8 MEI 2025 ID REG: EREG10043712400408-09

- Bila Anda berpotensi hamil, Anda harus menggunakan kontrasepsi yang efektif;
  - selama Anda menjalani pengobatan dengan TECENTRIQ® dan
  - sampai setidaknya 5 bulan sejak dosis terakhir.
- Sampaikan pada dokter Anda, bila Anda menjadi hamil saat sedang menjalani pengobatan dengan TECENTRIQ®.

Menyusui

Belum diketahui apakah TECENTRIQ® masuk ke dalam air susu ibu. Tanyakan pada dokter Anda apakah Anda sebaiknya berhenti menyusui atau Anda sebaiknya berhenti menjalani pengobatan dengan TECENTRIQ®.

Berkendara dan menggunakan mesin

TECENTRIQ® memiliki pengaruh yang kecil terhadap kemampuan Anda untuk berkendara atau menggunakan peralatan atau mesin. Bila Anda merasa lelah, jangan berkendara atau menggunakan peralatan atau mesin hingga Anda merasa lebih baik.

3. Cara pemberian TECENTRIQ®

Anda akan diberikan TECENTRIQ® oleh dokter yang berpengalaman di bidang pengobatan kanker di rumah sakit atau klinik.

Jumlah TECENTRIQ® yang diberikan

Untuk pengobatan kanker pada paru-paru, yang disebut kanker paru bukan sel kecil/*non-small cell lung cancer* (NSCLC), kanker paru sel kecil/*small cell lung cancer* (SCLC), kanker pada kandung kemih dan sistem kemih yang disebut ‘karsinoma urotelial’ dan kanker hati/*hepatocellular carcinoma* (HCC):

Dosis yang direkomendasikan adalah

- 840 miligram (mg) setiap dua minggu, atau
- 1200 miligram (mg) setiap tiga minggu, atau
- 1680 miligram (mg) setiap empat minggu.

Bagaimana cara pemberian TECENTRIQ®

TECENTRIQ® diberikan sebagai tetesan ke dalam pembuluh darah vena (disebut ‘infus intravena’ atau ‘IV’).

Infus pertama Anda akan diberikan dalam waktu 60 menit.

- Dokter Anda akan mengawasi Anda secara saksama selama infus pertama.
- Bila Anda tidak mengalami reaksi infus selama infus pertama, infus selanjutnya akan diberikan pada Anda selama periode 30 menit.

Berapa lama pengobatan berlangsung

Dokter Anda akan terus memberikan TECENTRIQ® hingga Anda tidak lagi mendapatkan manfaat dari obat tersebut. Namun, obat ini dapat dihentikan bila efek sampingnya tidak dapat ditangani dengan baik.

Bila Anda melewatkan dosis TECENTRIQ®

Bila Anda melewatkan jadwal berobat, segeralah menjadwalkannya kembali. Agar pengobatan dapat efektif sepenuhnya, sangat penting untuk tetap mendapatkan dosis TECENTRIQ® sesuai rekomendasi.

DISETUJUI OLEH BPOM 8 MEI 2025 ID REG: EREG10043712400408-09

Bila Anda berhenti menerima TECENTRIQ®

Jangan menghentikan pengobatan dengan TECENTRIQ® kecuali Anda telah mendiskusikan hal ini dengan dokter Anda. Hal ini disebabkan penghentian pengobatan dapat menghentikan efek dari obat ini.

Bila Anda memiliki pertanyaan lebih lanjut mengenai penggunaan obat ini, tanyakan pada dokter, apoteker atau perawat Anda.

4. Kemungkinan efek samping

Seperti semua obat-obatan, obat ini dapat menyebabkan efek samping, walaupun tidak semua pasien mengalaminya.

Segera sampaikan pada dokter, apoteker atau perawat Anda bila Anda menemukan efek samping manapun yang tertera di bawah ini atau bila terjadi pemburukan. Efek samping ini dapat terjadi dalam beberapa minggu atau beberapa bulan setelah dosis terakhir Anda. Jangan mencoba mengobati diri Anda sendiri dengan obat-obatan lain.

TECENTRIQ® terapi tunggal

Efek samping di bawah ini telah dilaporkan dalam uji klinis dengan TECENTRIQ® terapi tunggal:

Sangat umum: dapat terjadi pada lebih dari 1 dari 10 pasien

- Diare
- Mual
- Muntah
- Merasa sangat lelah dan tidak bertenaga (*fatigue*)
- Merasa lemas
- Demam
- Infeksi saluran kemih
- Penurunan nafsu makan
- Nyeri sendi
- Nyeri punggung
- Nyeri otot dan tulang
- Sakit kepala
- Batuk
- Sesak napas
- Ruam
- Gatal pada kulit

Umum: dapat terjadi pada hingga 1 dari 10 pasien

- Jumlah keping darah yang rendah, yang dapat membuat Anda lebih mudah untuk memar atau berdarah
- Defisiensi aktivitas kelenjar tiroid (hipotiroidisme)
- Sulit menelan
- Peradangan pada usus
- Nyeri perut
- Nyeri kerongkongan
- Menggigil

DISETUJUI OLEH BPOM 8 MEI 2025 ID REG: EREG10043712400408-09

- Gejala seperti flu
- Reaksi alergi (reaksi terkait infus atau hipersensitivitas)
- Peningkatan kadar enzim hati (ditemukan pada uji laboratorium) – dapat merupakan tanda dari peradangan pada hati
- Peradangan hati (hepatitis)
- Kadar kalium atau natrium rendah dalam darah (ditemukan pada pengujian)
- Kadar gula darah tinggi
- Peningkatan kreatinin darah
- Rendahnya kadar oksigen yang dapat menyebabkan napas tersengal-sengal yang merupakan akibat dari radang paru-paru (hipoksia)
- Peradangan pada paru-paru
- Nasofaringitis
- Kulit kering
- Tekanan darah rendah (hipotensi)
- Gangguan pada selaput pembungkus jantung (perikardium)
- Mulut kering (*dry mouth*)
- Kerusakan saraf yang mengakibatkan kemungkinan mati rasa, nyeri, dan/atau hilangnya fungsi motorik (neuropati perifer)

Tidak umum: dapat terjadi pada hingga 1 dari 100 pasien

- Kelenjar tiroid yang aktif secara berlebihan (hipertiroidisme)
- Kadar hormon adrenal yang rendah
- Diabetes melitus tipe 1
- Peradangan pankreas
- Peradangan jaringan otot (miositis)
- Kebas atau lumpuh – dapat merupakan gejala dari sindrom ‘Guillain-Barre’
- Peradangan pada selaput sekitar saraf tulang belakang dan otak
- Peradangan pada kulit yang ditandai dengan ruam merah, kulit kering, tebal, bersisik, dan mudah terkelupas
- Erupsi obat berat/*Severe Cutaneous Adverse Reactions* (SCARs)
- Peningkatan kreatin fosfokinase dalam darah (berdasarkan hasil tes), yang mungkin merupakan tanda peradangan pada otot atau jantung

Jarang: dapat terjadi pada hingga 1 dari 1000 pasien

- Peradangan pada otot jantung
- Peradangan pada kelenjar pituitari yang berada pada dasar otak
- Miastenia gravis – penyakit yang dapat menyebabkan kelemahan otot
- Peradangan pada ginjal (nefritis)
- Kelumpuhan pada otot-otot wajah yang diaktifkan oleh saraf wajah (*facial paresis*)
- Peradangan pada satu bagian saraf tulang belakang (myelitis)
- Gangguan sistem imun *haemophagocytic lymphohistiocytosis* (HLH)

DISETUJUI OLEH BPOM 8 MEI 2025 ID REG: EREG10043712400408-09

TECENTRIQ® terapi kombinasi

Efek samping di bawah ini telah dilaporkan dalam uji klinis TECENTRIQ® dengan kombinasi:

Sangat umum: dapat terjadi pada lebih dari 1 dari 10 pasien

- Jumlah sel darah merah rendah (anemia)
- Jumlah salah satu komponen sel darah putih rendah (neutropenia)
- Jumlah keping darah yang rendah (trombositopenia)
- Kerusakan saraf yang mengakibatkan kemungkinan mati rasa, nyeri, dan/atau hilangnya fungsi motorik (neuropati perifer)
- Jumlah sel darah putih rendah (leukopenia)
- Kelenjar tiroid yang kurang aktif (hipotiroidisme)
- Sembelit
- Pembengkakan pada bagian tubuh akibat menyimpan banyak cairan
- Infeksi paru-paru
- Nasofaringitis
- Kebotakan
- Hipertensi

Umum: dapat terjadi pada hingga 1 dari 10 pasien

- Jumlah sel darah putih limfosit turun (limfopenia)
- Sekresi kelenjar tiroid yang berlebihan (hipertiroidisme)
- Seriawan
- Peningkatan alkaline fosfatase darah
- Penurunan kadar magnesium dalam darah (hipomagnesemia)
- Pusing
- Gangguan indra pengecap
- Hilangnya kesadaran
- Adanya protein dalam urine (proteinurea)
- Perubahan suara yang abnormal

Tidak umum: dapat terjadi pada hingga 1 dari 100 pasien

- Kadar hormon adrenal yang rendah
- Peradangan pada kelenjar pituitari yang berada pada dasar otak
- Peradangan pada ginjal
- Erupsi obat berat/*Severe Cutaneous Adverse Reactions* (SCARs)

Bila Anda menemukan/merasakan efek samping manapun dari yang tertera di atas atau bila terjadi pemburukan, segera sampaikan pada dokter, apoteker atau perawat Anda.

Pelaporan efek samping

Bila Anda mengalami efek samping, beri tahu dokter, apoteker atau perawat Anda. Termasuk efek samping apa pun yang mungkin terjadi tetapi tidak tertera pada brosur ini. Anda juga dapat melaporkan efek samping langsung melalui:

PT Roche Indonesia – *Patient Safety*
Email: indonesia.safety@roche.com

DISETUJUI OLEH BPOM 8 MEI 2025 ID REG: EREG10043712400408-09

Tel: +62 21 3041 3000
Situs web: https://medinfo.roche.com/id/id.html

Dengan melaporkan efek samping, Anda dapat membantu memberikan lebih banyak informasi mengenai keamanan obat ini.

5. Cara penyimpanan TECENTRIQ®

TECENTRIQ® akan disimpan oleh tenaga kesehatan profesional di rumah sakit atau klinik. Rincian penyimpanan adalah sebagai berikut:

- Jauhkan obat ini dari pandangan dan jangkauan anak-anak.
- Jangan gunakan obat ini setelah melewati tanggal kedaluwarsa yang tertera pada dus dan label pada vial setelah "EXP". Tanggal kedaluwarsa merujuk pada hari terakhir dari bulan tersebut.
- Simpan dalam kulkas (2°C hingga 8°C). Jangan dibekukan.
- Simpan vial dalam dus pembungkus untuk melindungi dari sinar.
- Jika disiapkan dalam kondisi aseptik, cairan yang sudah dilarutkan tidak boleh disimpan lebih dari 30 hari pada 2°C hingga 8°C atau 24 jam pada suhu ruang.
- Jangan menggunakan obat ini jika keruh, berubah warna atau mengandung partikel.

Jangan membuang obat-obatan apa pun melalui saluran air atau pembuangan rumah tangga. Tenaga kesehatan profesional Anda akan membuang obat-obatan yang sudah tidak digunakan. Tindakan ini akan membantu melindungi lingkungan.

6. Isi kemasan dan informasi lain

Apa kandungan TECENTRIQ®

- Zat aktif berupa atezolizumab. Setiap mL mengandung 60 mg atezolizumab
  - vial mengandung atezolizumab 1200 mg (dalam 20 mL)
  - vial mengandung atezolizumab 840 mg (dalam 14 mL)
- Komposisi lainnya adalah L-histidin, asam asetat glasial, sukrosa, polisorbat 20, dan air untuk injeksi.

Tampilan TECENTRIQ® dan isi kemasan

TECENTRIQ® adalah konsentrat untuk larutan infus. Obat ini merupakan cairan jernih tidak berwarna hingga agak kekuningan.

TECENTRIQ® tersedia dalam kemasan berisi satu vial.

Kemasan yang terdaftar

Tecentriq 1200 mg/20 mL No. Reg.: DKI2157509949A1

Dus, 1 vial @ 20 mL

Tecentriq 840 mg/14 mL No. Reg.: DKI2157509949B1

Dus, 1 vial @ 14 mL

Obat: Jauhkan dari jangkauan dan pandangan anak-anak
Harus dengan resep dokter

DISETUJUI OLEH BPOM 8 MEI 2025 ID REG: EREG10043712400408-09

Pada proses pembuatannya bersinggungan dengan bahan bersumber babi.

Tecentriq 1200 mg/20 mL & Tecentriq 840 mg/14 mL

Diproduksi oleh:

F. Hoffman-La Roche Ltd., Kaiseraugst, Swiss

untuk F. Hoffman-La Roche Ltd., Basel, Swiss

Diimpor oleh:

PT Menarini Indria Laboratories, Bekasi, Indonesia

Didistribusikan oleh:

PT Roche Indonesia, Jakarta, Indonesia

This PIL draft has been reviewed and approved for submission by Pramelita and Lissa on 19-Nov-2024

DISETUJUI OLEH BPOM 8 MEI 2025 ID REG: EREG10043712400408-09