KEYNOTE-042 CLINICAL TRIAL SUMMARY

Please scan the QR code to access our MSD Connect healthcare professional website.

This website contains healthcare professional and patient resources, clinical study summaries, and more.

KEYTRUDA® (pembrolizumab) is a Prescription Medicine and is available as a 100 mg/4 mL concentrate for solution for infusion.

Please review the KEYTRUDA Data Sheet before prescribing. The Data Sheet is available at www.medsafe.govt.nz.

INDICATIONS: In combination with pemetrexed and platinum chemotherapy for first-line treatment of metastatic non-squamous non-small cell lung carcinoma (NSCLC), with no EGFR or ALK genomic tumour aberrations. In combination with carboplatin and either paclitaxel or nab-paclitaxel for first-line treatment of metastatic squamous NSCLC. As monotherapy for first-line treatment of patients with NSCLC whose tumours express PD-L1 [tumour proportion score (TPS) ≥1%] as determined by a validated test, with no EGFR or ALK genomic tumour aberrations and are either; metastatic, or stage III where patients are not candidates for surgical resection or definitive chemoradiation. As monotherapy for the treatment of patients with advanced NSCLC with a PD-L1 TPS level ≥1% as determined by a validated test and who have received platinum-containing chemotherapy. Patients with EGFR or ALK genomic tumour aberrations should have received prior therapy for these aberrations prior to receiving KEYTRUDA. As monotherapy for the adjuvant treatment of patients with Stage IB (T2a ≥4 cm), II, or IIIA NSCLC who have undergone complete resection. See Data Sheet for other indications.

CONTRAINDICATIONS: Hypersensitivity to the active substance or to any of the excipients listed in section 6.1 of the Data Sheet. See Data Sheet for further information.

PRECAUTIONS: Severe and fatal cases of immune-mediated adverse reactions have occurred. Immune-related adverse reactions have occurred after discontinuation of treatment with KEYTRUDA and can affect more than one body system simultaneously. For management of immune-mediated adverse reactions, see Data Sheet. Immune-mediated adverse reactions have occurred as follows: pneumonitis (including fatal cases), colitis, hepatitis, nephritis, adrenal insufficiency, hypophysitis, type 1 diabetes mellitus, hyperthyroidism, hypothyroidism, thyroiditis, severe skin reactions (Stevens-Johnson syndrome and toxic epidermal necrolysis [including fatal cases], bullous pemphigoid), uveitis, myositis, Guillain-Barre syndrome, pancreatitis, encephalitis, sarcoidosis, myasthenic syndrome/myasthenia gravis (including exacerbation), myelitis, vasculitis, hypoparathyroidism, gastritis, haemolytic anaemia, pericarditis, myocarditis, sclerosing cholangitis, exocrine pancreatic insufficiency, solid organ transplant rejection, acute graft-versus-host-disease (GVHD) including fatal GVHD with a history of allogeneic hematopoietic stem cell transplantation, higher than expected frequencies of Grades 3 and 4 ALT and AST elevations in advanced RCC when used in combination with axitinib, increased mortality when in combination with dexamethasone and a thalidomide analogue in multiple myeloma (not indicated), severe infusion reactions including hypersensitivity and anaphylaxis. Monitor thyroid and liver function. Limited data in patients with active infections and with history of severe adverse reaction to ipilimumab – use caution. No data in severe renal impairment, or moderate or severe hepatic impairment. Pregnancy (Category D). See Data Sheet for further information.

INTERACTIONS: None expected. Avoid systemic corticosteroids or immunosuppressants prior to treatment (except as premedication in combination with chemotherapy).

ADVERSE EVENTS: Monotherapy: pneumonitis, colitis, diarrhoea, pyrexia, fatigue, pruritus, rash, nausea, hypothyroidism, hyperthyroidism, adrenal insufficiency, hepatitis, hypophysitis, nephritis, type 1 diabetes mellitus, arthralgia, cough, back pain, vitiligo, lymphopenia, hypertriglyceridemia, abdominal pain, hyponatremia, hyperglycaemia, hypoalbuminemia, increased AST and ALP, anaemia, dyspnoea, constipation, increased lipase; Combination (where not already listed under Monotherapy) *with chemotherapy:* alopecia, asthenia, decreased neutrophil count, neutropenia, thrombocytopenia, mucosal inflammation, stomatitis, vomiting, decreased white blood cell count, decreased appetite, decreased platelet count. See Data Sheet for further information.

DOSAGE AND ADMINISTRATION: Adults: 200 mg every 3 weeks or 400 mg every 6 weeks. Paediatrics (see Indications): 2 mg/kg (up to 200 mg) every 3 weeks. Administered as an intravenous infusion over 30 minutes. For use in combination, please reviaew the Data Sheets for KEYTRUDA and the relevant concomitant therapies. KEYTRUDA should be administered first when given in combination with intravenous chemotherapy. Treat with KEYTRUDA until disease progression or unacceptable toxicity. Atypical responses (i.e. an initial transient increase in tumour size or small new lesions followed by shrinkage) have been observed. Clinically stable patients (i.e. asymptomatic and not requiring urgent intervention) with initial evidence of progression can remain on treatment until confirmed. For the adjuvant treatment of NSCLC, treat with KEYTRUDA for up to one year or until disease recurrence or unacceptable toxicity. See Data Sheet for further information. (v54.02)

KEYTRUDA is funded for the first-line treatment of patients with advanced or metastatic NSCLC. Further restrictions apply, see pharmac.govt.nz.[4]

KEYTRUDA is unfunded for the other NSCLC indications - a charge will apply.

References: 1. KEYTRUDA Data Sheet. **2.** Mok TSK, Wu YL, Kudaba I, *et al. Lancet.* 2019;393(10183):1819–1830. **3.** de Castro G, Kudaba I, Wu YL, *et al. J Clin Oncol.* 2023;41(11):1986–1991. **4.** PHARMAC. Pharmaceutical Schedule. Available at: https://pharmac.govt.nz/pharmaceutical-schedule Accessed 30 October 2024.

ALK: anaplastic lymphoma kinase; **ECOG PS:** Eastern Cooperative Oncology Group performance status; **EGFR:** epidermal growth factor receptor; **HR:** hazard ratio; **mNSCLC:** metastatic non-small-cell lung cancer; **NSCLC:** non-small cell lung cancer; **ORR:** objective response rate; **OS:** overall survival; **PD-L1:** programmed death ligand 1; **PFS:** progression-free survival; **Q3W:** every 3 weeks; **RECIST:** Response Evaluation Criteria in Solid Tumours; **TPS:** tumour proportion score.

Merck Sharp & Dohme (New Zealand) Limited. Level 3, 123 Carlton Gore Road, Newmarket, Auckland.
NZ-LAM-00056v12.0. TAPS DA 2422PC. Issued March 2025. MSD13500.

MSD

KEYTRUDA®
(pembrolizumab)

KEYTRUDA is indicated as monotherapy for the first-line treatment of patients with NSCLC expressing PD-L1 [tumour proportion score (TPS) ≥1%] as determined by a validated test, with no EGFR or ALK genomic tumour aberrations, and is stage III where patients are not candidates for surgical resection or definitive chemoradiation, or metastatic.[1]

A Key to More Tomorrows is Possible for your Appropriate Patients with Locally Advanced/Metastatic NSCLC*[1,2]

*Superior **OVERALL SURVIVAL** (PD-L1 TPS ≥1%) with **KEYTRUDA** vs. platinum-containing chemotherapy: **HR 0.81 (95% CI: 0.71–0.93), p=0.002.**[1] Median follow-up of 12.8 months.[2]

INCLUDES 5-YEAR FOLLOW-UP DATA FOR KEYNOTE-042

Edward, 63 years

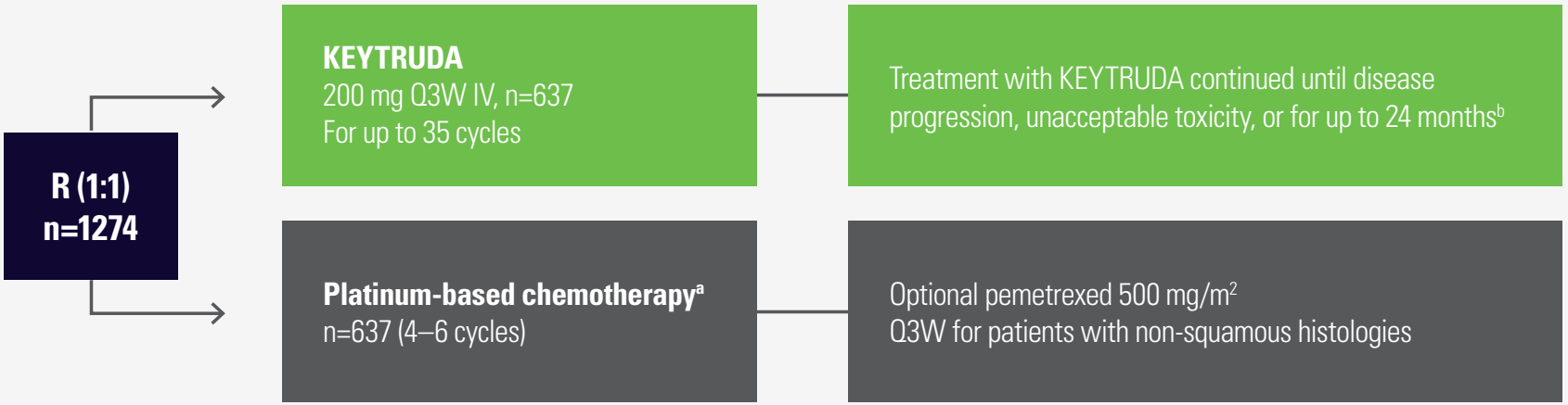
- Locally advanced NSCLC, and not a candidate for surgical resection or definitive chemoradiation
- No prior history of treatment for advanced disease
- PD-L1 TPS 74%
- ECOG performance status: 1
- Smoking status: 17-pack-year history, quit 11 years ago

Hypothetical patient

IN PATIENTS WITH STAGE III NSCLC WHO WERE NOT CANDIDATES FOR SURGICAL RESECTION OR DEFINITIVE CHEMORADIATION OR mNSCLC WITH PD-L1 TPS ≥1% AND NO EGFR OR ALK GENOMIC TUMOUR ABERRATIONS

KEYNOTE-042 Study Design[1,2]

A phase 3, randomised, multicentre, active-controlled trial in patients with stage III NSCLC who were not candidates for surgical resection or definitive chemoradiation, or patients with metastatic NSCLC.[1,2]



Exclusion criteria included autoimmune disease that required systemic therapy within 2 years of treatment; a medical condition that required immunosuppression; or patients who had received more than 30 Gy of thoracic radiation within the prior 26 weeks were ineligible.[1,2]

Key eligibility criteria

- Adults ≥18 years
- PD-L1 TPS of ≥1%
- Previously untreated locally advanced or metastatic non-small cell lung cancer
- No sensitising EGFR/ALK genomic tumour aberrations
- ECOG PS 0 or 1
- Life-expectancy 3 months or longer

Primary efficacy endpoint:

Overall survival.

Secondary efficacy endpoints:

Progression-free survival (PFS) and objective response rate (ORR).

a. Investigator's choice of platinum containing chemotherapy included pemetrexed 500 mg/m^2 Q3W and carboplatin AUC 5–6 mg/mL/min Q3W for a maximum of 6 cycles; paclitaxel 200 mg/m^2 and carboplatin AUC 5–6 mg/ML/min Q3W for a maximum of 6 cycles. Patients with non-squamous NSCLC could receive pemetrexed maintenance.[2]

b. Administration of KEYTRUDA was permitted beyond RECIST-defined disease progression if the patient was clinically stable and considered to be deriving clinical benefit by the investigator. Treatment with KEYTRUDA could be reinitiated for subsequent disease progression and administered for up to 1 additional year.[2]

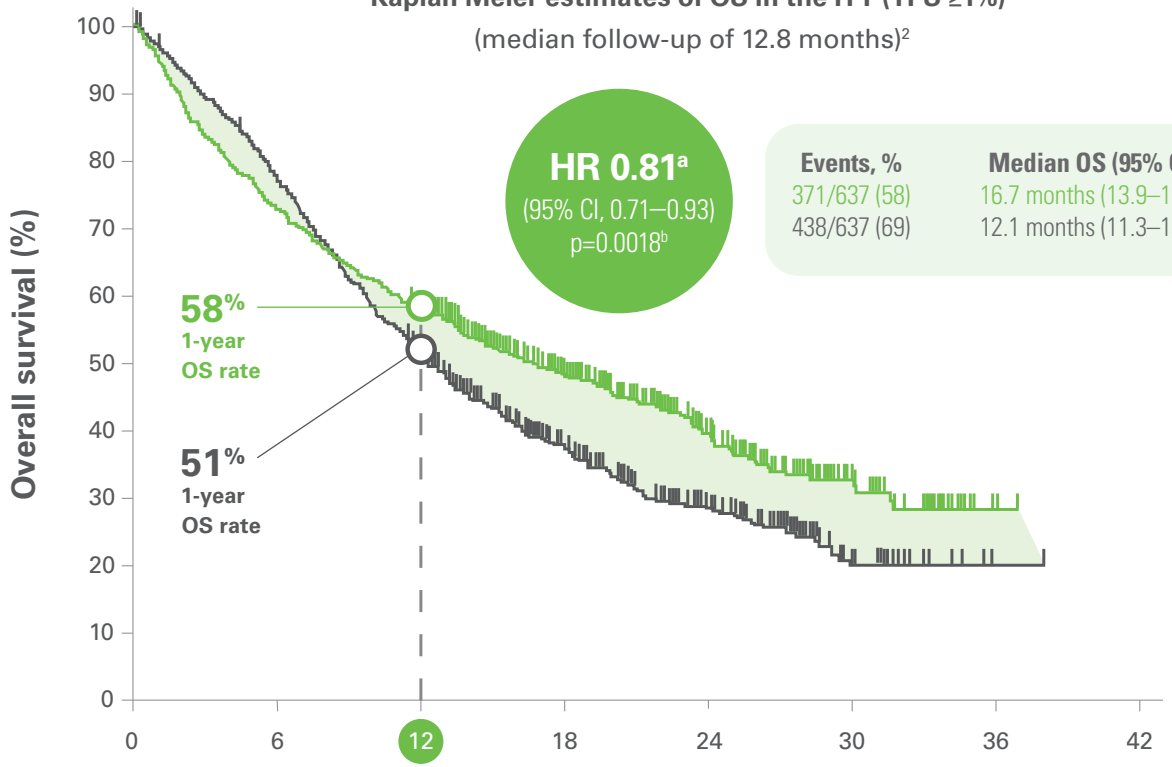
IN PATIENTS WITH STAGE III NSCLC WHO WERE NOT CANDIDATES FOR SURGICAL RESECTION OR DEFINITIVE CHEMORADIATION OR mNSCLC WITH PD-L1 TPS ≥1% AND NO EGFR OR ALK GENOMIC TUMOUR ABERRATIONS

KEYNOTE-042: Overall survival at median follow-up of 12.8 months[1,2]

SUPERIOR OVERALL SURVIVAL (OS)*

***HR 0.81, 95% CI: 0.71–0.93, p=0.0018 for KEYTRUDA vs. platinum-based chemotherapy[1]**

Kaplan Meier estimates of OS in the ITT (TPS ≥1%)[1]
(median follow-up of 12.8 months)[2]



Events, %	Median OS (95% CI)
371/637 (58)	16.7 months (13.9–19.7)
438/637 (69)	12.1 months (11.3–13.3)

No. at risk

KEYTRUDA	637	463	365	214	112	35	2	0
Platinum-based Chemotherapy	637	463	316	166	88	24	0	0

Adapted from KEYTRUDA Data Sheet.[1]

a. Hazard ratio (KEYTRUDA compared to chemotherapy) based on the stratified Cox proportional hazard model.
b. Based on stratified log-rank test.

OS in co-primary endpoints for KEYTRUDA vs. chemotherapy[2]

PD-L1 TPS ≥50%, (n=599)[2]

HR 0.69[a]
(95% CI, 0.56–0.85)
p=0.0003[b]

PD-L1 TPS ≥20%, (n=818)[2]

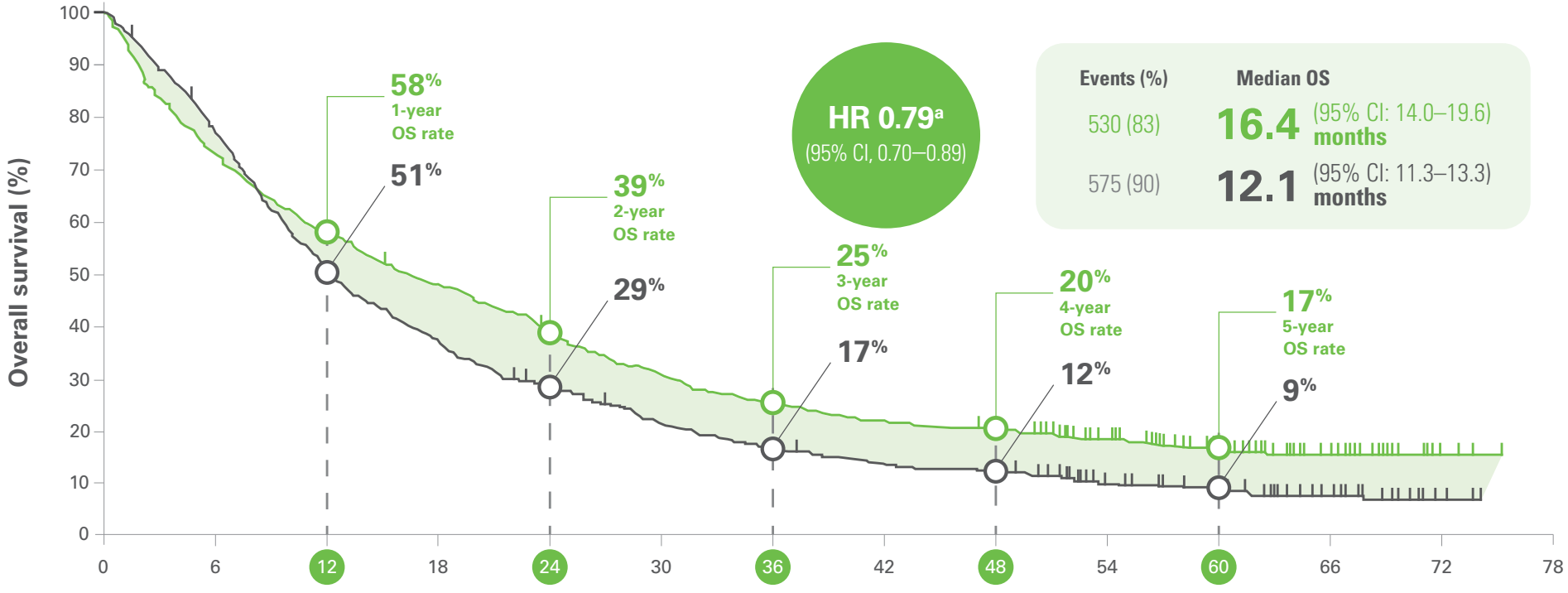
HR 0.77[a]
(95% CI, 0.64–0.92)
p=0.0020[b]

IN PATIENTS WITH STAGE III NSCLC WHO WERE NOT CANDIDATES FOR SURGICAL RESECTION OR DEFINITIVE CHEMORADIATION OR mNSCLC WITH PD-L1 TPS ≥1% AND NO EGFR OR ALK GENOMIC TUMOUR ABERRATIONS

KEYNOTE-042: Overall survival PD-L1 TPS ≥1% (median follow-up time: 61.1 months)[1-3]

LIMITATION: This post-hoc analysis (median follow-up time: 61.1 months) for KEYNOTE-042 was exploratory in nature. No formal statistical testing was planned for the updated analysis and, therefore, no statistical conclusions can be drawn.[2,3]

Kaplan Meier estimates of OS in the ITT (TPS ≥1%) (exploratory analysis; median follow-up: 61.1 months)[3]



No. at risk

KEYTRUDA	637	463	368	304	246	193	160	137	127	93	59	28	3	0
Platinum-based Chemotherapy	637	485	319	236	178	131	103	83	75	46	33	17	3	0

Adapted from de Castro G, *et al. J Clin Oncol.* 2023.[3]

a. HR based on the stratified Cox proportional hazard model with the Efron method of tie handling.

IN PATIENTS WITH STAGE III NSCLC WHO WERE NOT CANDIDATES FOR SURGICAL RESECTION OR DEFINITIVE CHEMORADIATION OR mNSCLC WITH PD-L1 TPS ≥1% AND NO EGFR OR ALK GENOMIC TUMOUR ABERRATIONS

KEYNOTE-042: Treatment-related adverse events in as-treated patients[3]

(median follow-up time: 61.1 months)

Adverse events (AEs) in the as-treated population

	KEYTRUDA (n = 636)		Chemotherapy (n = 615)	
Any treatment-related AE, n (%)	406 (63.8)		555 (90.2)	
Grade 3–5	120 (18.9)		257 (41.8)	
Led to treatment discontinuation	58 (9.1)		59 (9.6)	
Led to death	13 (2.0)		14 (2.3)	
Occurring in ≥10% of patients in either treatment group	Any Grade	Grade 3–5	Any Grade	Grade 3–5
Hypothyroidism	69 (10.8)	1 (0.2)	2 (0.3)	0
Fatigue	51 (8.0	3 (0.5)	103 (16.7)	8 (1.3)
Decreased appetite	40 (6.3)	5 (0.8)	108 (17.6)	8 (1.3)
Anemia	35 (5.5)	4 (0.6)	234 (38.0)	85 (13.8)
Nausea	31 (4.9)	0	185 (30.1)	7 (1.1)
Vomiting	15 (2.4)	0	97 (15.8)	2 (0.3)
Constipation	8 (1.3)	0	69 (11.2)	0
Neutropenia	5 (0.8)	1 (0.2)	89 (14.5)	47 (7.6)
Decreased white blood cells	3 (0.5)	0	75 (12.2)	34 (5.5)
Alopecia	2 (0.3)	0	136 (22.1)	7 (1.1)
Decreased neutrophil count	2 (0.3)	0	89 (14.5)	56 (9.1)
Decreased platelet count	2 (0.3)	0	66 (10.7)	22 (3.6)

Immune-mediated AEs and infusion reactions[a]

	KEYTRUDA (n = 636)		Chemotherapy (n = 615)	
	Any Grade	Grade 3–5	Any Grade	Grade 3–5
Any AE, n (%)	175 (27.5)	52 (8.2)	47 (7.6)	9 (1.5)
Hypothyroidism	77 (12.1)	1 (0.2)	10 (1.6)	0
Pneumonitis	52 (8.2)	21 (3.3)	3 (0.5)	1 (0.2)
Hyperthyroidism	38 (6.0)	1 (0.2)	4 (0.7)	0
Severe skin reactions	14 (2.2)	11 (1.7)	2 (0.3)	1 (0.2)
Thyroiditis	10 (1.6)	0	0	0
Hepatitis	9 (1.4)	7 (1.1)	0	0
Infusion reactions	9 (1.4)	0	27 (4.4)	6 (1.0)
Colitis	8 (1.3)	5 (0.8)	2 (0.3)	1 (0.2)
Adrenal insufficiency	4 (0.6)	2 (0.3)	1 (0.2)	0
Hypophysitis	3 (0.5)	3 (0.5)	0	0
Nephritis	3 (0.5)	1 (0.2)	0	0
Pancreatitis	1 (0.2)	1 (0.2)	0	0
Myocarditis	1 (0.2)	1 (0.2)	0	0
Uveitis	0	0	1 (0.2)	0

a. Events were based on a list of terms specified at the time of analysis and were included regardless of attribution to study treatment or immune relatedness by the investigator. Related terms were included.

No new safety signals were identified at this longer follow-up[3]

KEYTRUDA RECOMMENDED DOSING IN mNSCLC[1]

DOSING AND SPECIAL POPULATIONS

KEYTRUDA RECOMMENDED DOSING IN mNSCLC[1]

As an IV infusion over 30 minutes[1]

- For use in combination, see the prescribing information for the concomitant therapies. When administering KEYTRUDA as part of a combination with intravenous chemotherapy, KEYTRUDA should be administered first.[1]
- Patients with NSCLC should be treated with KEYTRUDA until disease progression or unacceptable toxicity, or for up to 24 months.[1]
- Atypical responses (i.e. an initial transient increase in tumour size or small new lesions followed by shrinkage) have been observed. Clinically stable patients (i.e. asymptomatic and not requiring urgent intervention) with initial evidence of progression can remain on treatment until confirmed. **See Data Sheet for further information.[1]**

SPECIAL POPULATIONS

Renal Insufficiency

No dose adjustment is needed for patients with mild or moderate renal impairment. KEYTRUDA has not been studied in patients with severe renal impairment.[1]

Hepatic Insufficiency

No dose adjustment is needed for patients with mild hepatic impairment. KEYTRUDA has not been studied in patients with moderate or severe hepatic impairment.[1]

Elderly

No overall differences in safety or efficacy were reported between elderly patients (65 years and over) and younger patients (less than 65 years). No dose adjustment is necessary in this population.[1]

Withhold or discontinue KEYTRUDA to manage adverse reactions as described in the Data Sheet.[1]