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 review 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.** Paz-Ares L *et al. N Engl J Med* 2018; 379: 2040–2051. **3.** Novello S, *et al. J Clin Oncol.* 2023;41(11):1999–2006. **4.** PHARMAC. Pharmaceutical Schedule. Available at: https://pharmac.govt.nz/pharmaceutical-schedule Accessed 30 October 2024.

BICR: blinded independent central review; **carbo:** carboplatin; **DoR:** duration of response; **HSCT:** haematopoietic stem cell transplant; **ITT:** intention to treat; **mNSCLC:** metastatic non-small cell lung cancer; **nab-pac:** nab-paclitaxel; **NR:** not reached; **ORR:** objective response rate; **OS:** overall survival; **pac:** paclitaxel; **PD-L1:** programmed death ligand 1; **pem:** pemetrexed; **PFS:** progression-free survival; **plat:** platinum therapy; **PK:** pharmacokinetic; **Q1W:** every week; **Q3W:** every 3 weeks; **Q6W:** every 6 weeks; **SJS:** Stevens-Johnson syndrome; **TEN:** toxic epidermal necrolysis; **TPS:** tumour proportion score.

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MSD

KEYTRUDA®
(pembrolizumab)

KEYTRUDA in the first-line treatment of patients with squamous mNSCLC

A Key To More Tomorrows Is Possible*[1,2]

***KEYTRUDA + carbo + pac/nab-pac** vs placebo + carbo + pac/nab-pac: **OVERALL SURVIVAL**; number of events 85/278 (31%) vs 120/281 (43%): **HR 0.64, 95% CI: 0.49–0.85, p=0.0008;** median follow-up of 7.8 months.[1,2]

INCLUDES 5-YEAR FOLLOW-UP DATA FOR KEYNOTE-407

Hypothetical patient

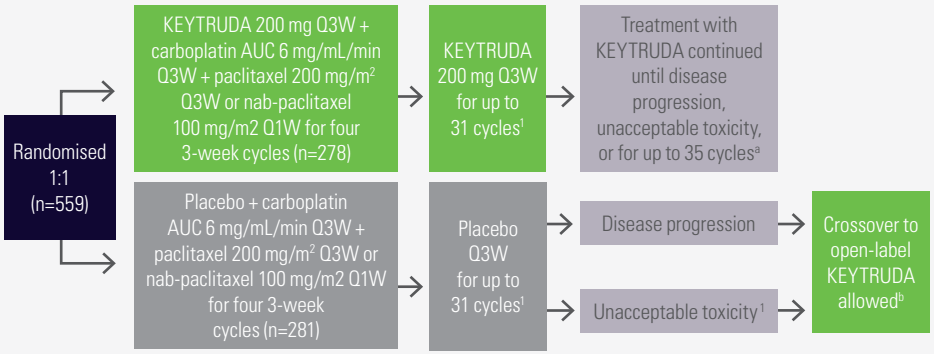
Linda, 70 years

- Stage IV squamous cell mNSCLC
- PD-L1 expression (TPS <50%)
- ECOG performance status: 1

IN FIRST-LINE SQUAMOUS mNSCLC WITH OR WITHOUT PD-L1 EXPRESSION

KEYNOTE-407 study design[1,2]

Phase 3, randomised, multicentre, double-blind, placebo-controlled study in previously untreated patients with squamous mNSCLC[2]



Key eligibility criteria[2]

- No prior systemic treatment of metastatic disease
- Pathologically confirmed Stage IV squamous NSCLC
- ECOG PS 0 or 1
- Provided a tumour sample for the determination of PD-L1 status

a. 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.[2]

b. Patients in the placebo + carbo + pac/nab-pac arm who had disease progression verified by BICR per RECIST v1.1 could cross over to receive KEYTRUDA as monotherapy.[2]

Primary endpoints:
OS and PFS (assessed by BICR per RECIST v1.1).[2]

Secondary efficacy endpoints:
ORR and DoR (both assessed by BICR per RECIST v1.1), and safety.[2]

- Patients were stratified by tumour PD-L1 status (TPS <1%; TPS ≥1%), paclitaxel or nab-paclitaxel, and geographic region.[2]
- Patients with an 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 26 weeks were ineligible.[1,2]

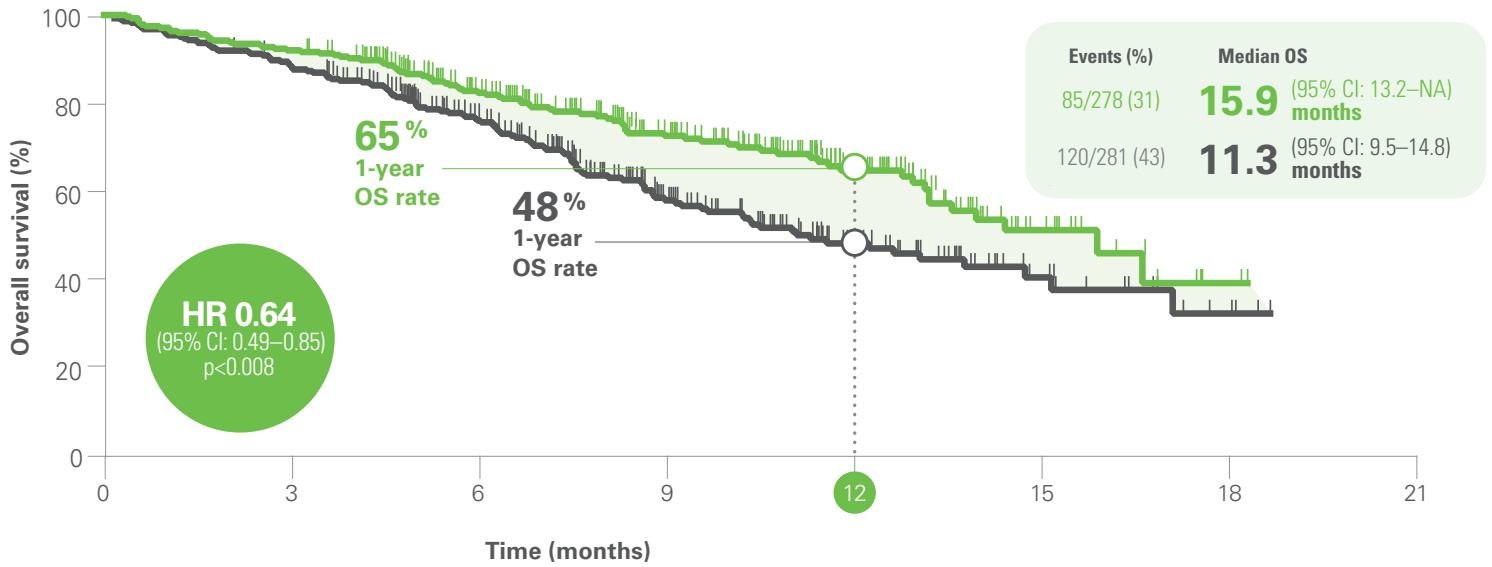
IN FIRST-LINE SQUAMOUS mNSCLC WITH OR WITHOUT PD-L1 EXPRESSION

KEYNOTE-407: Proven efficacy across endpoints at median follow-up of 7.8 months[2]

SUPERIOR OVERALL SURVIVAL (OS)*

***HR 0.64, 95% CI: 0.49–0.85, p<0.0008** for KEYTRUDA + carbo + pac/nab-pac vs. placebo + carbo + pac/nab-pac[1]

Kaplan-Meier estimates of OS (ITT) in initial analysis of KEYNOTE-407[1,2]



No. at risk								
KEYTRUDA + carbo + pac/nab-pac	278	256	188	124	62	17	2	0
Placebo + carbo + pac/nab-pac	281	246	175	93	45	16	4	0

Adapted from Paz-Ares L *et al.* 2018.[2]

HR based on the stratified Cox proportional hazard model; p-value based on stratified log-rank test.

SUPERIOR PROGRESSION-FREE SURVIVAL (PFS)†

†**HR 0.56**, 95% CI: 0.45–0.70, p<0.0001 for KEYTRUDA + carbo + pac/nab-pac (number of events 152/278 [55%]) vs placebo + carbo + pac/nab-pac (number of events 197/281 [70%])[1]

SUPERIOR OBJECTIVE RESPONSE RATE (ORR) (secondary endpoint)‡

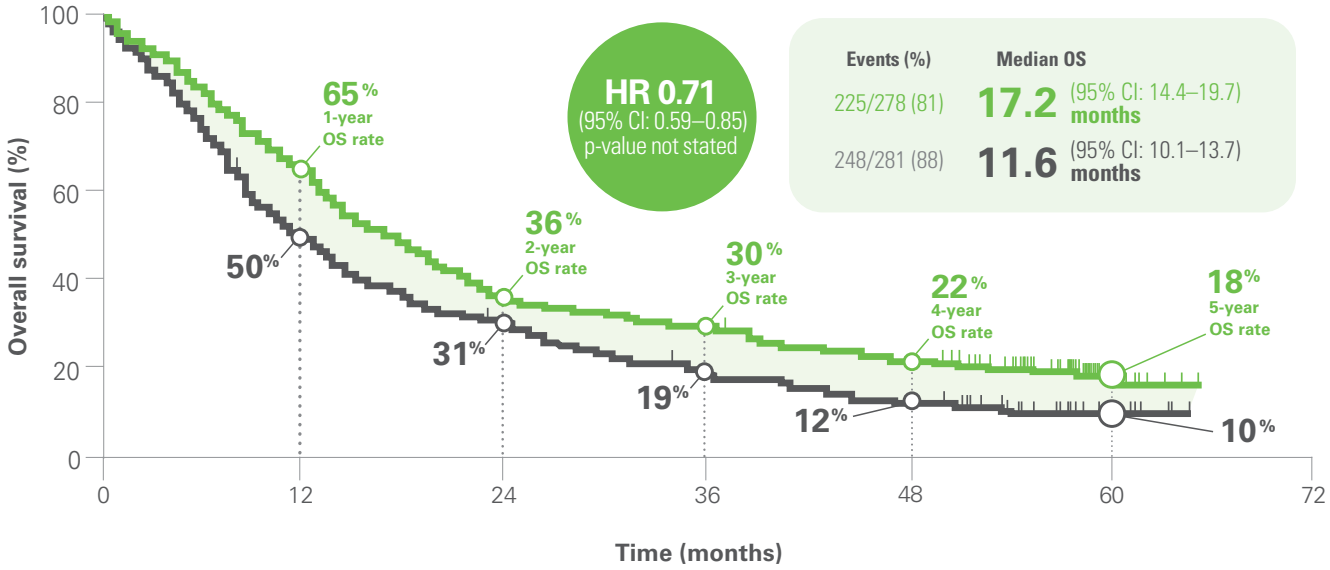
‡**58% ORR** (95% CI: 48–68) for KEYTRUDA + carbo + pac/nab-pac (n=101) vs 35% (95% CI: 26–45) for placebo + carbo + pac/nab-pac (n=102); p=0.0004 at the initial interim analysis[1]

IN FIRST-LINE SQUAMOUS mNSCLC WITH OR WITHOUT PD-L1 EXPRESSION

KEYNOTE-407: Overall survival at median follow-up of 56.9 months[3]

LIMITATION: No formal statistical testing was planned at this post hoc exploratory analysis therefore no statistical conclusions can be drawn.

Kaplan-Meier estimates of OS (ITT) in exploratory analysis of KEYNOTE-407[3]



No. at risk

KEYTRUDA + carbo + pac/nab-pac	278	180	100	83	60	10	0
Placebo + carbo + pac/nab-pac	281	137	84	50	33	7	0

Adapted from Novello S, *et al. J Clin Oncol.* 2023.[3]

OS in PD-L1 subgroups (exploratory analyses) for KEYTRUDA + carbo + pac/nab-pac vs placebo + carbo + pac/nab-pac

Without PD-L1 expression

HR 0.83 (95% CI: 0.61–1.13) — **TPS <1%**, n=194[3]

With PD-L1 expression

HR 0.61 (95% CI: 0.45–0.83) — **TPS 1–49%**, n=207[3]

HR 0.68 (95% CI: 0.47–0.97) — **TPS ≥50%**, n=146[3]

LIMITATION: KEYNOTE-407 was not powered to detect treatment effect differences in these subgroups; therefore results from these exploratory analyses should be interpreted with caution because of the modest patient numbers and potential imbalances in baseline characteristics within the subgroups.

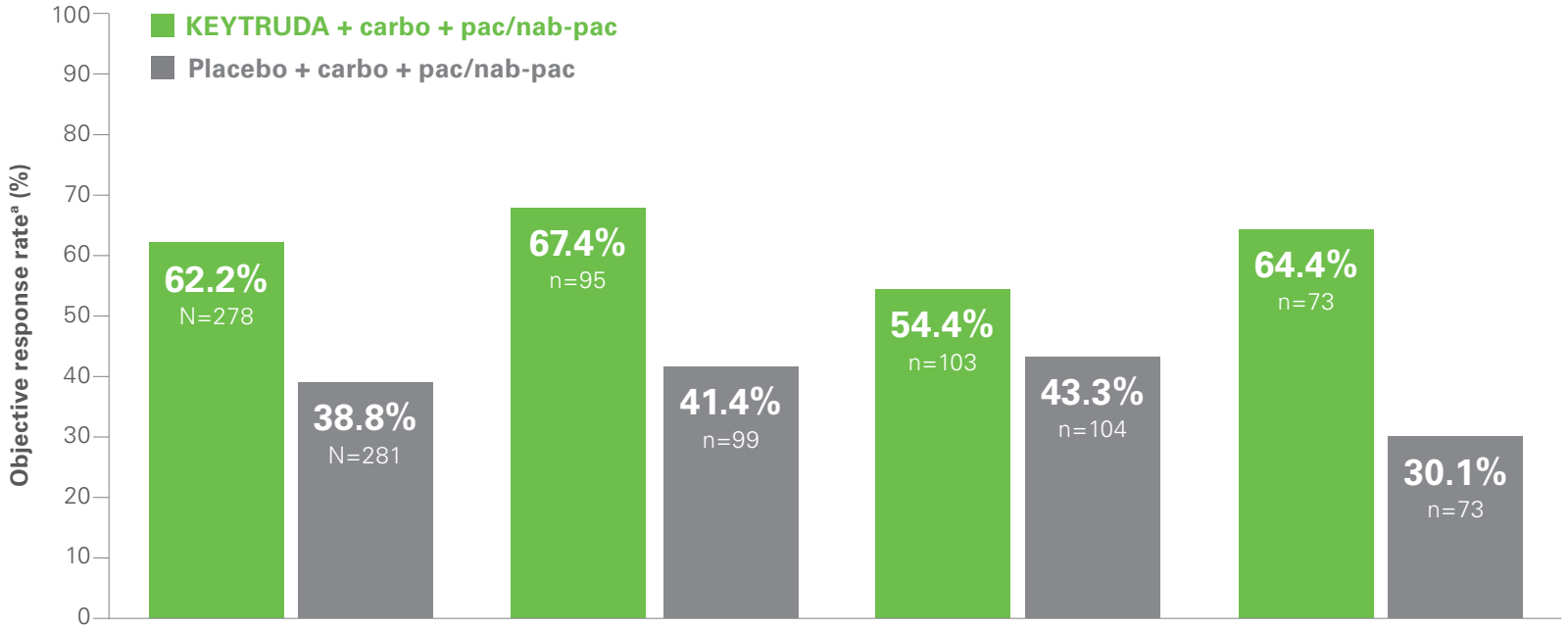
IN FIRST-LINE SQUAMOUS mNSCLC WITH OR WITHOUT PD-L1 EXPRESSION

KEYNOTE-407: Response rates (secondary endpoint) at median follow-up of 56.9 months[3]

LIMITATION: No formal statistical testing was planned at this post hoc exploratory analysis therefore no statistical conclusions can be drawn.

Tumour response rates in updated exploratory analysis of KEYNOTE-407[3]

(p-values not available)



Median DoR[b] months (range)	**9.0** (1.3+ to 61.5+)	**4.9** (1.3+ to 58.6+)	**6.9** (1.4+ to 58.9+)	**5.7** (1.4+ to 55.8+)	**11.1** (1.3+ to 61.5+)	**4.8** (2.0 to 58.6+)	**10.4** (2.7 to 59.4+)	**4.6** (1.3+ to 58.6+)

In patients who completed 35 cycles of KEYTRUDA in updated analysis of KEYNOTE-407 (n=55)[3]

ORR[a]
91% (95% CI: 80.0–97.0)

CR
16% (n=9)

PR
75% (n=41)

Median DoR[b]
Not reached
(range 7.1 to 61.5+ months)

Alive without PD or subsequent therapy
44% (n=24)

a. Per RECIST v1.1 by BICR. b. Kaplan-Meier estimate.

Novello S, *et al. J Clin Oncol.* 2023.[3]

KEYNOTE-407: Safety profile

In squamous mNSCLC with or without PD-L1 expression

Summary of adverse events (AEs) in KEYNOTE-407 (as-treated population) at median follow-up of 56.9 months[3]

	KEYTRUDA + carbo + pac/nab-pac (n=278)	Placebo + carbo + pac/nab-pac (n=280)
Any AEs, n (%)	274 (98.6)	275 (98.2)
Grade 3–5	208 (74.8)	196 (70.0)
Led to discontinuation		
Any treatment	80 (28.8)	37 (13.2)
All treatments[a]	48 (17.3)	21 (7.5)
Led to death	32 (11.5)	20 (7.1)
Any treatment-related AE that led to death	12 (4.3)[b]	5 (1.8)[c]
Immune-mediated AEs and infusion reactions, n (%)	99 (35.6)	26 (9.3)
Grade 3–5	37 (13.3)	9 (3.2)

All 55 patients who completed 35 cycles of KEYTRUDA had an AE (all treatment-related), and 35 (63.6%) had grade 3/4 AEs (no deaths). Immune-mediated AEs and infusion reactions occurred in 21 patients (38.2%; one grade 3 event).[3]

AEs were monitored from random assignment through 30 days (90 days for serious AEs) after treatment cessation and graded according to the National Cancer Institute Common Terminology Criteria for Adverse Events, version 4.0.

a. Includes patients who discontinued pembrolizumab or placebo, carboplatin, and taxane owing to an AE at any time and patients who discontinued pembrolizumab or placebo owing to an AE after completing four 3-week cycles of carboplatin and taxane.

b. Including sepsis, n=3; death (cause not specified), n=2; cardiac arrest, cardiac failure, hepatic failure, necrotizing fasciitis, pneumonitis, pulmonary hemorrhage, and respiratory failure, n=1 each.

c. Including septic shock, n=2; pneumonia, acute renal injury, and pulmonary hemorrhage, n=1 each.

Adapted from Adapted Novello S, *et al. J Clin Oncol.* 2023.[3]

- **The most frequent AEs of any grade reported in ≥15%** of patients in the KEYTRUDA + carbo + pac/nab-pac arm were anaemia, alopecia, neutropenia, nausea, diarrhoea, thrombocytopenia, decreased appetite, arthralgia, constipation, fatigue, asthenia, peripheral neuropathy, rash, pruritus, vomiting, cough, pyrexia, and dyspnoea.[3] Refer to the Data Sheet for further safety information.
- **The most frequent grade 3-5 AEs reported in ≥1%** of patients in the KEYTRUDA + carbo + pac/nab-pac arm were neutropenia (23.0%), anaemia (15.8%), thrombocytopenia (8.3%), fatigue (4.7%), diarrhoea (4.3%), decreased appetite (2.5%), asthenia (2.2%), arthralgia (1.8%), dyspnoea (1.4%), nausea (1.4%), peripheral neuropathy (1.1%), and immune-mediated AEs and infusion reactions (13.3%).[3]
- **Incidence of immune-mediated AEs occurring in >1% (any grade)** with KEYTRUDA + carbo + pac/nab-pac were hypothyroidism (12.2%), pneumonitis (8.3%), hyperthyroidism (7.6%), infusion reactions (5.4%), colitis (3.2%), hepatitis (2.2%), severe skin reactions (2.2%), hypophysitis (1.4%), and thyroiditis (1.1%).[3]

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.[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]