Prescribing information GB | NI

KEYTRUDA® (pembrolizumab) plus carboplatin and paclitaxel for the first-line treatment of patients with metastatic squamous NSCLC: A clinical perspective

KEYTRUDA®, in combination with carboplatin and either paclitaxel or nab-paclitaxel, is indicated for the first-line treatment of metastatic squamous non-small cell lung carcinoma in adults[1]

Explore the case study

Adverse events should be reported. Reporting forms and information can be found at https://yellowcard.mhra.gov.uk/ or search for MHRA Yellow Card in the Google Play or Apple App Store. Adverse events should also be reported to MSD (Tel: 0208 154 8000).

Refer to the Summary of Product Characteristics before prescribing KEYTRUDA® to help minimise the risks associated with treatment.[1]
Prescribing information can be found at the top of each page in the document.

MSD

KEYTRUDA® (pembrolizumab)

This case study is for UK healthcare professionals only. The patient provided consent for the case to be shared. Please note that this is one individual patient and cases may vary.

NSCLC, non-small cell lung carcinoma; **PD-L1**, programmed death-ligand 1; **TPS**, tumour proportion score.

1. KEYTRUDA® Summary of Product Characteristics. Available at: https://www.medicines.org.uk/emc/product/2498. Accessed June 2023.

GB-PDO-02599 | June 2023

Merck Sharp & Dohme (UK) Limited, 120 Moorgrate, London, EC2M 6UR

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Meet Fred

Age: 67 years
Occupation: Manual worker
Personal life: Married with children

Presenting complaint: Slight weight loss, reduced appetite, and worsening lethargy

Diagnosis: Metastatic squamous NSCLC

How could choosing immunotherapy (IO) combination in first-line help patients like Fred with metastatic squamous NSCLC and a PD-L1 TPS <1%?

The links to the prescribing information at the top of each page directs users to an external website.
NSCLC, non-small cell lung cancer; **PD-L1**, programmed death-ligand 1; **TPS**, tumour proportion score.

KEYTRUDA® (pembrolizumab)

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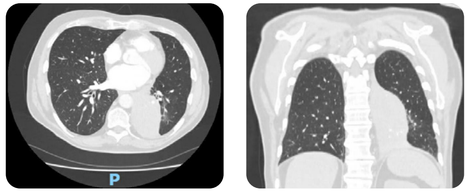
Fred, 67 years old
Occupation: Manual worker
Personal life: Married with children

Presenting complaint:
Slight weight loss, reduced appetite, and worsening lethargy

Medical history:
Ex-smoker with COPD;
Previously treated with salbutamol and beclomethasone inhalers;
Congenital absence of right kidney;
Tongue cancer removed in 2008;
Hearing loss;
Dry cough since EBUS

CT images*



DEC 2021

Diagnosis

EBUS revealed
T4 N3 M1a† (pleural effusion) squamous cell lung cancer
- Biomarker testing: TPS <1%; PD-L1 0%

FEB 2022

Fred's wife and daughter always attended his consultations

Fred has ECOG PS1 and still continues to work but finds he needs to sit down more often

Explore more

What first-line treatment options are available for patients like Fred?

The links to the prescribing information at the top of each page directs users to an external website.
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*Images were provided by the treating physician.
†The Tumour, Node and Metastasis (TNM) system is a cancer staging system.[1] This patient case was diagnosed with stage 4 tumour (T4), stage 3 lymph node involvement (N3) and stage 1a distant metastasis (M1a).
COPD, chronic obstructive pulmonary disease; **CT**, computerised tomography; **EBUS**, endobronchial ultrasound; **ECOG**, Eastern Cooperative Oncology Group; **PD-L1**, programmed death-ligand 1; **PS1**, performance status 1; **TPS**, tumour proportion score.
1. Cancer Research UK. TNM staging for lung cancer. Available at: https://www.cancerresearchuk.org/about-cancer/what-is-cancer/stages-of-cancer#tnm. Accessed June 2023.

KEYTRUDA® (pembrolizumab)

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Fred, 67 years old
Diagnosis: Squamous NSCLC

- Biomarker testing: TPS <1%; PD-L1 0%

Explore KEYTRUDA® combination therapy outcomes in the KEYNOTE-407 study and the rationale for selecting this treatment for Fred

IO + chemotherapy

MAR 2022
Starts first-line KEYTRUDA®[1] + carboplatin + paclitaxel

APR 2022
Rapid increase of cardiac biomarkers

- proBNP increased from 30 pg/mL to 223 pg/mL during first cycle of treatment

APR 2022
Treatment continued and proBNP trend monitored

MAY 2022
proBNP level decreased to 166 pg/mL

MAY 2022
Cycle 3 of treatment continued

MAY 2022
Partial response determined by CT

SEPT 2022
Ongoing tumour shrinkage determined by CT

SEPT 2022
proBNP levels decreased to 56 pg/mL

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Explore more

The links to the prescribing information at the top of each page directs users to an external website.
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CT, computerised tomography; **IO**, immunotherapy; **NSCLC**, non-small cell lung carcinoma; **PD-L1**, programmed death-ligand 1; **proBNP**; pro B-type natriuretic peptide; **TPS**, tumour proportion score.
1. KEYTRUDA® Summary of Product Characteristics. Available at: https://www.medicines.org.uk/emc/product/2498. Accessed June 2023.

KEYTRUDA® (pembrolizumab)

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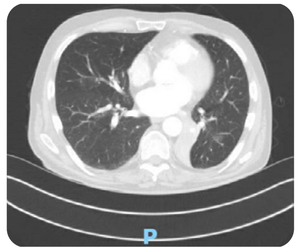
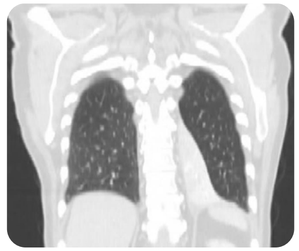
Fred, 67 years old
Diagnosis: Squamous NSCLC

- Biomarker testing: TPS <1%; PD-L1 0%

How would you manage these adverse events?

CT images*





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SEPT 2022
New onset of loose stools (Grade 2 colitis)

FEB 2023

MAR 2023
proBNP levels decreased to 47 pg/mL

MAR 2023
Ongoing radiological response

MAR 2023
Grade 2 colitis stable

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*Images were provided by the treating physician.
CT, computerised tomography; **NSCLC**, non-small cell lung carcinoma; **PD-L1**, programmed death-ligand 1; **proBNP**; pro B-type natriuretic peptide; **TPS**, tumour proportion score.

KEYTRUDA® (pembrolizumab)

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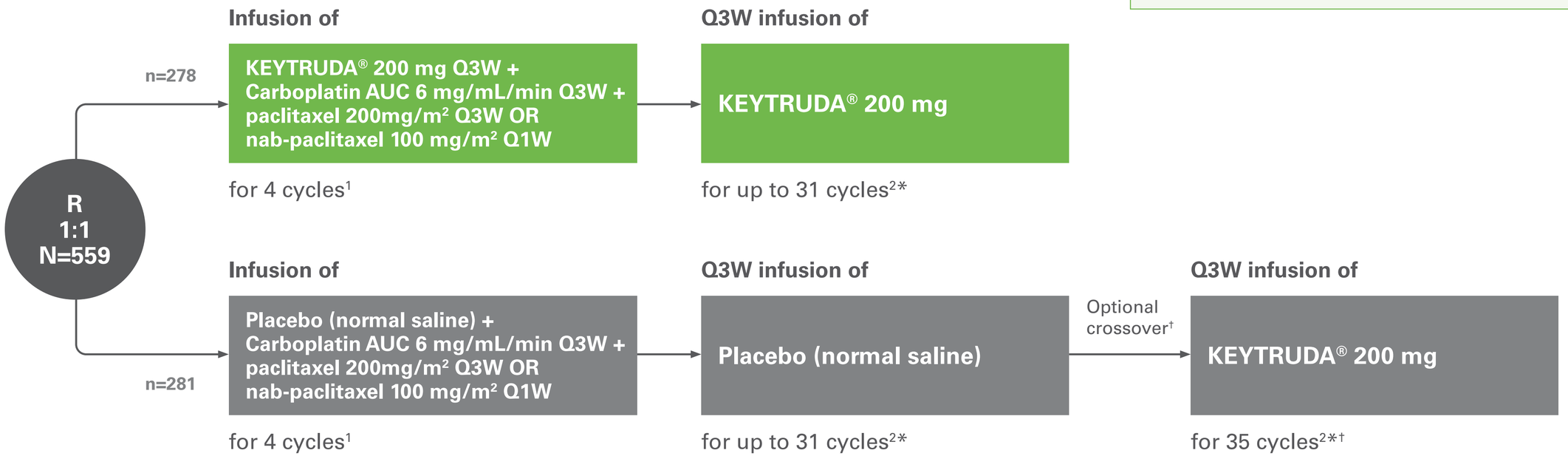
KEYNOTE-407 trial with KEYTRUDA®: Study design[1,2]

KEYNOTE-407 is a **randomised, double-blind, active-controlled, phase 3 trial** in patients with previously untreated stage IV, squamous NSCLC.[1]

The primary endpoints of this study were **overall survival** and **progression-free survival**.[1]

Inclusion criteria[1]:
- ≥18 years of age
- Untreated stage IV, squamous NSCLC



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*Treatment continued until radiographic disease progression was confirmed by blinded, independent central review per RECIST version 1.1, unacceptable toxicity, investigator's decision, or withdrawal of patient consent.
†To be eligible for crossover to KEYTRUDA® monotherapy, disease progression had to have been verified by blinded, independent, central radiologist review and all safety criteria had to have been met.[2]
AUC, area under the curve; **ELCC**, European Lung Cancer Congress; **NSCLC**, non-small cell lung carcinoma; **Q1W**, every week; **Q3W**, every 3 weeks; **R**, randomisation; **RECIST**, Response Evaluation Criteria in Solid Tumors.
1. Paz-Ares L, et al. *New Eng J Med.* 2018;379:2040–2051; 2. Robinson AG, et al. Presented at ELCC 2021. 25–27 March 2021, Virtual.

KEYTRUDA® (pembrolizumab)

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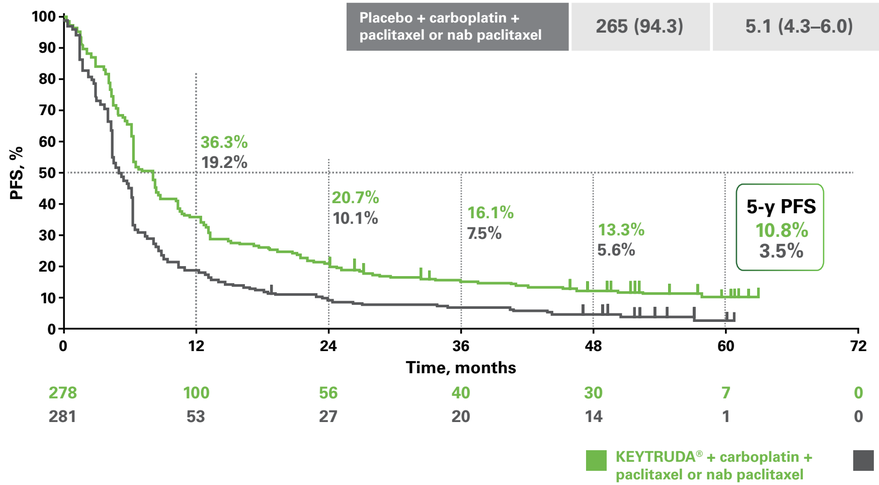
Patients treated with KEYTRUDA® combination therapy had a greater PFS benefit compared with the placebo group at 7.8 months median follow-up with the trend towards treatment benefit maintained at 5 years: data from the KEYNOTE-407 trial

AT 7.8 MONTHS
(median follow-up)

PFS* was greater among patients in the **KEYTRUDA®** combination group, with a **44% reduced risk of progression or death** compared with the placebo group **(HR: 0.56; 95% CI: 0.45–0.70; p<0.001)**.[1]

At 5 years, KEYTRUDA® combination therapy continued to demonstrate a trend towards treatment benefit[2†]

	Events n (%)	Median (95% CI)	HR (95% CI)
KEYTRUDA® + carboplatin + paclitaxel or nab paclitaxel	241 (86.7)	8.0 (6.3–8.5)	0.62 (0.52–0.74) p = not tested
Placebo + carboplatin + paclitaxel or nab paclitaxel	265 (94.3)	5.1 (4.3–6.0)	



56.9 months
Median follow-up

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*PFS and ORR were assessed by blinded, independent central review per RECIST version 1.1.
†Exploratory analysis; significance was not tested and no statistical conclusions can be drawn from this analysis.
CI, confidence interval; **HR**, hazard ratio; **NSCLC**, non-small cell lung carcinoma; **ORR**, overall response rate; **PFS**, progression-free survival; **RECIST**, Response Evaluation Criteria in Solid Tumors.
1. Paz-Ares L, et al. *New Eng J Med.* 2018;379:2040–2051; 2. Novello S, et al. Presented at the ESMO meeting, 9–13 September 2022, Paris, France and Virtual.

KEYTRUDA® (pembrolizumab)

Prescribing information GB | NI

Patients treated with KEYTRUDA® combination therapy had a greater OS benefit compared with the placebo group at 7.8 months median follow-up with the trend towards treatment benefit maintained at 5 years: data from the KEYNOTE-407 trial

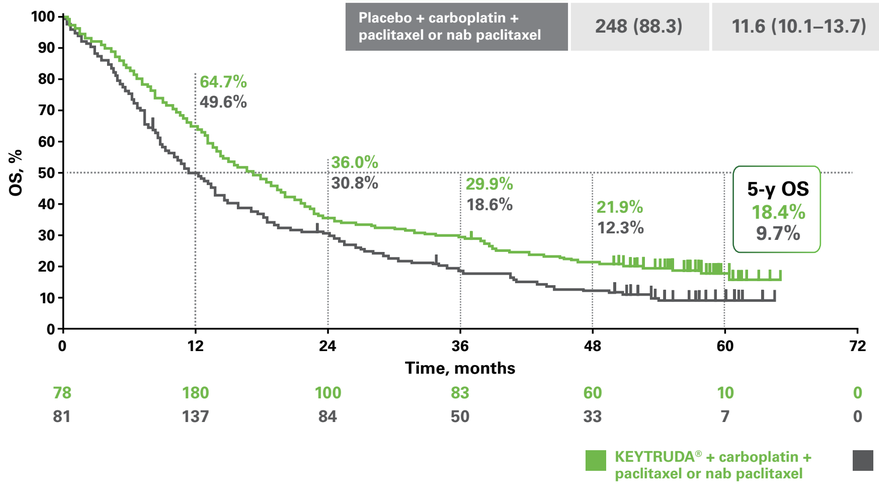
AT 7.8 MONTHS
(median follow-up)

OS was greater among patients in the **KEYTRUDA®** combination group, with a **36% reduced risk of death** compared with the placebo group **(HR: 0.64; 95% CI: 0.49–0.85; p<0.001)**.[1]

What was the rationale for selecting this treatment for Fred?

At 5 years, KEYTRUDA® combination therapy continued to demonstrate a trend towards treatment benefit[2]*

	Events n (%)	Median (95% CI)	HR (95% CI)
KEYTRUDA® + carboplatin + paclitaxel or nab paclitaxel	225 (80.9)	17.2 (14.4–19.7)	0.71 (0.59–0.85) p = not tested
Placebo + carboplatin + paclitaxel or nab paclitaxel	248 (88.3)	11.6 (10.1–13.7)	



56.9 months
Median follow-up

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*Exploratory analysis; significance was not tested and no statistical conclusions can be drawn from this analysis.
CI, confidence interval; **HR**, hazard ratio; **NSCLC**, non-small cell lung carcinoma; **OS**, overall survival; **RECIST**, Response Evaluation Criteria in Solid Tumors.
1. Paz-Ares L, et al. *New Eng J Med.* 2018;379:2040–2051; 2. Novello S, et al. Presented at the ESMO meeting, 9–13 September 2022, Paris, France and Virtual.

KEYTRUDA® (pembrolizumab)

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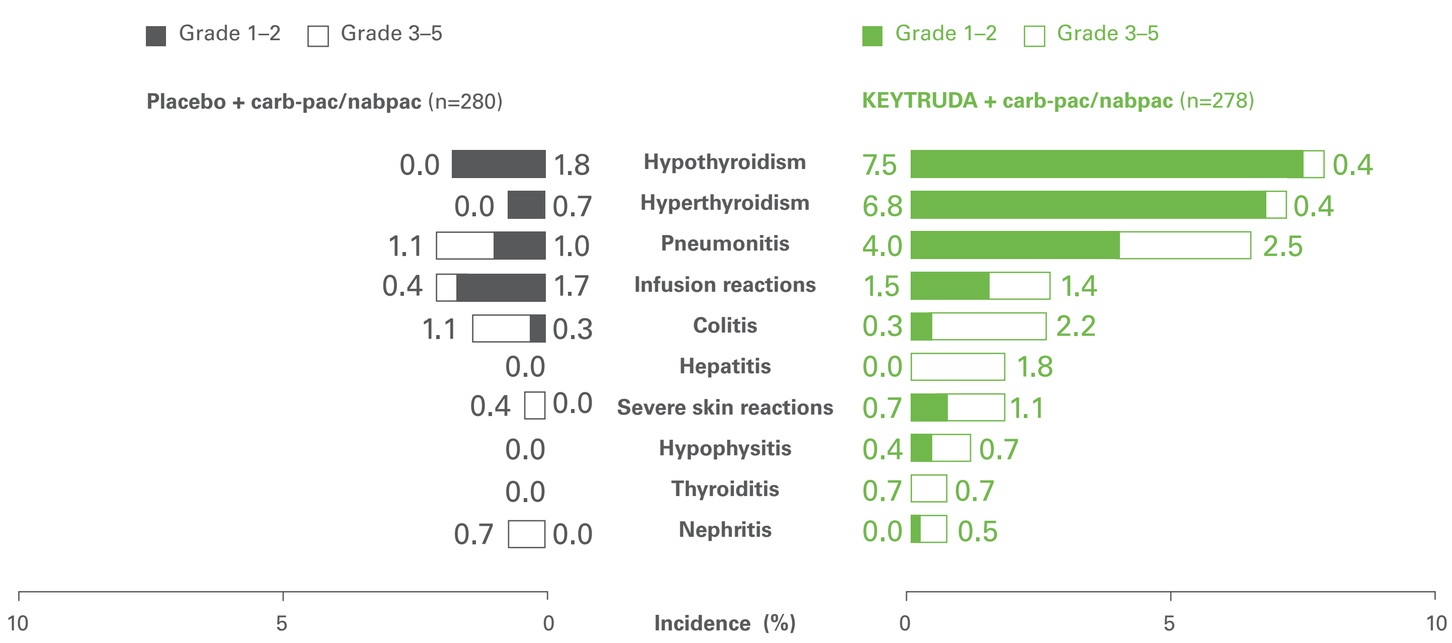
Immune-mediated AEs with KEYTRUDA® combination therapy at 7.8 months median follow-up: data from the KEYNOTE-407 trial (original analysis)*†

AT 7.8 MONTHS
(median follow-up)



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*Regardless of attribution to a trial drug by the investigator.
†AEs were graded according to the National Cancer Institute Common Terminology Criteria for Adverse Events, Version 4.0.
AE, adverse event.
1. Paz-Ares L, et al. *New Eng J Med.* 2018;379:2040–2051.

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Patients treated with KEYTRUDA® combination therapy had manageable toxicity at 5 years[1], consistent with previous reports: data from the KEYNOTE-407 trial (follow-up analysis)

AT 56.9 MONTHS
(median follow-up)

Adverse event, n (%)	All treated patients		35 cycles of KEYTRUDA® n = 55
	KEYTRUDA® + carboplatin + paclitaxel or nab paclitaxel n = 278	Placebo + carboplatin + paclitaxel or nab paclitaxel n = 280	
Any	274 (98.6)	275 (98.2)	55 (100)
Grade 3–5	208 (74.8)	196 (70.0)	35 (63.6)
Led to treatment discontinuation*			
Any treatment	80 (28.8)	37 (13.2)	3 (5.5)
All treatments	48 (17.3)	21 (7.5)	0
Led to death	32 (11.5)	20 (7.1)	0
Immune-mediated AEs and infusion reactions†	99 (35.6)	26 (9.3)	21 (38.2)
Grade 3–5	37 (13.3)	9 (3.2)	1 (1.8)

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*Includes patients who discontinued KEYTRUDA® or placebo, carboplatin and taxane owing to any AE at any time and patients who discontinued KEYTRUDA® or placebo, carboplatin and taxane owing to an AE after completing four 3-week cycles of carboplatin and taxane.
†Events considered regardless of attribution to treatment or immune relatedness by the investigator.
AE, adverse event.
1. Novello S, et al. Presented at the ESMO meeting, 9–13 September 2022, Paris, France and Virtual.

KEYTRUDA® (pembrolizumab)

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What treatment options are available to patients like Fred?

Patients with squamous NSCLC whose tumours have no targetable mutations are eligible for the following first-line treatment options in England and Wales[1*†]

Combination IO + chemotherapy[1]

For patients like Fred with **no targetable mutations or PD-L1<50%**, this would include:[1]

KEYTRUDA®[2] + carboplatin + paclitaxel

Chemotherapy alone[1]

For patients like Fred with **no targetable mutations or PD-L1<50%**, this would include:[1]

Platinum doublet chemotherapy

All treatment choices are based on shared decisions between patient and clinician[1]

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*The treatment options stated were from NICE guidance last updated in March 2023.[1] Please refer to the NICE/Blueteq guidelines for the most up to date information.
†In Scotland, the first-line treatment options for squamous NSCLC are combination IO plus chemotherapy (KEYTRUDA®[2] + carboplatin + paclitaxel) or chemotherapy alone (pemetrexed plus platinum chemotherapy).[3,4]
IO, immunotherapy; **NSCLC**, non-small cell lung carcinoma; **PD-L1**, programmed death-ligand 1.

1. NICE Guidance NG122. September 2022. Available at: https://www.nice.org.uk/guidance/ng122/resources/interactive-pdf-of-all-treatment-pathways-for-squamous-and-nonsquamous-advanced-nonsmallcell-lung-cancer-pdf-11189888174. Accessed June 2023; 2. KEYTRUDA® Summary of Product Characteristics. Available at: https://www.medicines.org.uk/emc/product/2498. Accessed June 2023; 3. SMC guidance SMC2187. September 2019. Available at: https://www.scottishmedicines.org.uk/medicines-advice/pembrolizumab-keytruda-full-smc2187/. Accessed June 2023; 4. SMC guidance 531/09. February 2009. Available at https://www.scottishmedicines.org.uk/medicines-advice/pemetrexed-alimta-fullsubmission-53109/. Accessed June 2023.

KEYTRUDA® (pembrolizumab)

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How were these AEs managed?

Raised proBNP levels during treatment cycle 2

KEYTRUDA® treatment was continued based on clinical experience of the treating physician and proBNP levels were regularly monitored

If the patient had Grade 3 or Grade 4 myocarditis, **KEYTRUDA®** treatment should be discontinued[1]

Please note: local and national guidelines for the management of AEs should be followed

Grade 2 colitis during treatment cycle 3

KEYTRUDA® prescribing information recommends withholding **KEYTRUDA®** for Grade 2 or Grade 3 colitis and administering corticosteroids for Grade ≥ 2 events[1]

If the patient had Grade 4 or recurrent Grade 3 colitis, **KEYTRUDA®** treatment should be discontinued[1†]

In the Keynote-407 trial, colitis (any grade) occurred more frequently in the KEYTRUDA arm than in the placebo arm (3.2% vs 1.4%)[2]

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*For further information on recommended treatment modifications for KEYTRUDA®, please refer to Table 1 in section 4.2 Posology and method of administration in the KEYTRUDA® SmPC.[1]
†For further information on immune-related colitis, please refer to section 4.4 Special warnings and precautions for use in the KEYTRUDA® SmPC.[1]
AE, adverse event; **MRI**, magnetic resonance imaging; **OD**, once daily; **proBNP**; pro B-type natriuretic peptide.
1. KEYTRUDA® Summary of Product Characteristics. Available at: https://www.medicines.org.uk/emc/product/2498. Accessed June 2023; 2. Paz-Ares, et al. *J Thorac Oncol.* 2020;15(10):1657–1669.

KEYTRUDA® (pembrolizumab)

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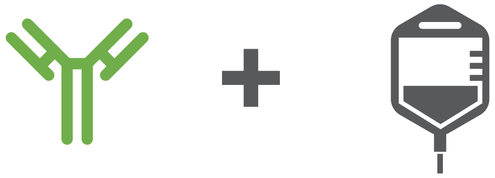
What was the rationale for selecting this treatment for Fred?

KEYTRUDA®[1] + carboplatin + paclitaxel



has a longer overall survival and progression-free survival than chemotherapy alone therefore was considered a suitable treatment option[2,3]

In addition, the following factors meant KEYTRUDA® combination therapy was a suitable option for Fred:

- PD-L1 TPS <50%
- ECOG PS1 at initial presentation

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ECOG, Eastern Cooperative Oncology Group; **PD-L1**, programmed death-ligand 1; **PS1**, performance status 1; **TPS**, tumour proportion score.
1. KEYTRUDA® Summary of Product Characteristics. Available at: https://www.medicines.org.uk/emc/product/2498. Accessed June 2023; 2. Paz-Ares L, et al. *New Eng J Med.* 2018;379:2040–2051; 3. NICE Guidance NG122. September 2022. Available at: https://www.nice.org.uk/guidance/ng122/resources/interactive-pdf-of-all-treatment-pathways-for-squamous-and-nonsquamous-advanced-nonsmallcell-lung-cancer-pdf-11189888174. Accessed June 2023.

KEYTRUDA® (pembrolizumab)