LIBTAYO®
(cemiplimab-rwlc)
Injection 350 mg

A FIRST-LINE TREATMENT OPTION IN ADVANCED NSCLC

LIBTAYO is indicated for the first-line treatment of patients with non–small cell lung cancer (NSCLC) whose tumors have high PD-L1 expression [tumor proportion score (TPS) ≥50%] as determined by an FDA-approved test, with no EGFR, ALK, or ROS1 aberrations, and is[1]:

- **Locally advanced where patients are not candidates for surgical resection or definitive chemoradiation or[1]**
- **Metastatic[1]**

Overall survival with LIBTAYO vs platinum-based chemotherapy in EMPOWER-Lung 1[1-3]*

ITT patient population (N=710)[1]

Median OS: 22.1 months
(95% CI, 17.7-NE) vs 14.3 months
(95% CI, 11.7-19.2) (chemotherapy†),
HR=0.68, *P*=0.0022[1]

32% reduction in risk of death; HR=0.68, *P*=0.0022[1]

Number of deaths: 30% of patients (108 out of 356 patients) with LIBTAYO and 40% of patients (141 out of 354 patients) with chemotherapy[1]

The EMPOWER-Lung 1 study was designed to enroll patients with PD-L1 ≥50%.[2]

- A total of 710 patients were enrolled and randomized. For some patients, it was later determined that PD-L1 biomarker testing was not conducted according to the instructions for use, and required retesting[2]
- An analysis was conducted in a subset of patients with known PD-L1 ≥50% (n=563). The analysis excluded 91 patients from the overall population whose PD-L1 status was unknown because their tumors could not be retested, and 56 patients from the overall population who had <50% PD-L1 expression[2] (LIBTAYO is not indicated in patients with <50% PD-L1 expression)

Known PD-L1 ≥50% patient population (n=563)[2,3]

Median OS: NR
(95% CI, 17.9-NE) vs 14.2 months
(95% CI, 11.2-17.5) (chemotherapy†),
HR=0.57, *P*=0.0002[2,3]

43% reduction in risk of death; HR=0.57, *P*=0.0002[2,3]

Number of deaths: 25% of patients (70 out of 283 patients) with LIBTAYO and 38% of patients (105 out of 280 patients) with chemotherapy[2,3]

PD-L1 expression was determined using the PD-L1 IHC 22C3 pharmDx assay.[1-3]

*Investigator's choice: Paclitaxel + cisplatin or carboplatin; gemcitabine + cisplatin or carboplatin; or pemetrexed + cisplatin or carboplatin followed by optional pemetrexed maintenance in patients with nonsquamous histology.[1-4]

†Platinum-based.[1-3]

ALK=anaplastic lymphoma kinase; EGFR=epidermal growth factor receptor; HR=hazard ratio; IHC=immunohistochemistry; ITT=intention-to-treat; NE=not evaluable; NR=not reached; OS=overall survival; PD-L1=programmed death receptor ligand 1; ROS1=ROS proto-oncogene 1, receptor tyrosine kinase.

Important Safety Information

Warnings and Precautions

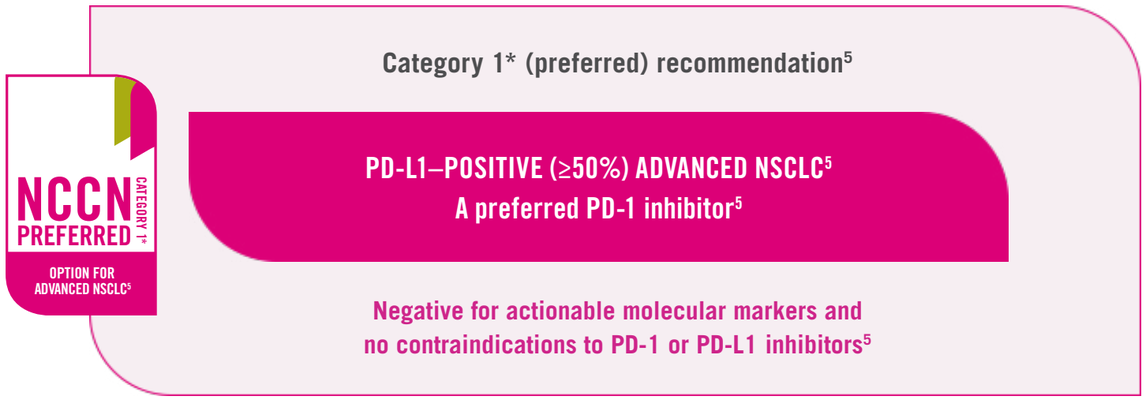
Severe and Fatal Immune-Mediated Adverse Reactions

Immune-mediated adverse reactions, which may be severe or fatal, can occur in any organ system or tissue at any time after starting treatment. While immune-mediated adverse reactions usually occur during treatment, they can also occur after discontinuation.

Please see additional Important Safety Information throughout and click here for full Prescribing Information.

NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®)[5]

NCCN Guidelines for Non-Small Cell Lung Cancer recommend cemiplimab-rwlc (LIBTAYO) as a Category 1* (preferred) systemic therapy option for advanced NSCLC[5†]



- Cemiplimab-rwlc (LIBTAYO) is 1 of 2 PD-1 inhibitors recommended in the NCCN Guidelines as a preferred (Category 1*) first-line monotherapy treatment for advanced NSCLC[5]

***Category 1 recommendation is based upon high-level evidence and uniform NCCN consensus that the intervention is appropriate.[5]**

†See the NCCN Guidelines for the detailed recommendations, including other preferred options.

NCCN makes no warranties of any kind whatsoever regarding their content, use, or application, and disclaims any responsibility for their application or use in any way.

Important Safety Information (continued)

Warnings and Precautions (continued)

Severe and Fatal Immune-Mediated Adverse Reactions (continued)

Immune-mediated adverse reactions affecting more than one body system can occur simultaneously. Early identification and management are essential to ensuring safe use of PD-1/PD-L1–blocking antibodies. The definition of immune-mediated adverse reactions included the required use of systemic corticosteroids or other immunosuppressants and the absence of a clear alternate etiology. Monitor closely for symptoms and signs that may be clinical manifestations of underlying immune-mediated adverse reactions. Evaluate liver enzymes, creatinine, and thyroid function at baseline and periodically during treatment. In cases of suspected immune-mediated adverse reactions, initiate appropriate workup to exclude alternative etiologies, including infection. Institute medical management promptly, including specialty consultation as appropriate.

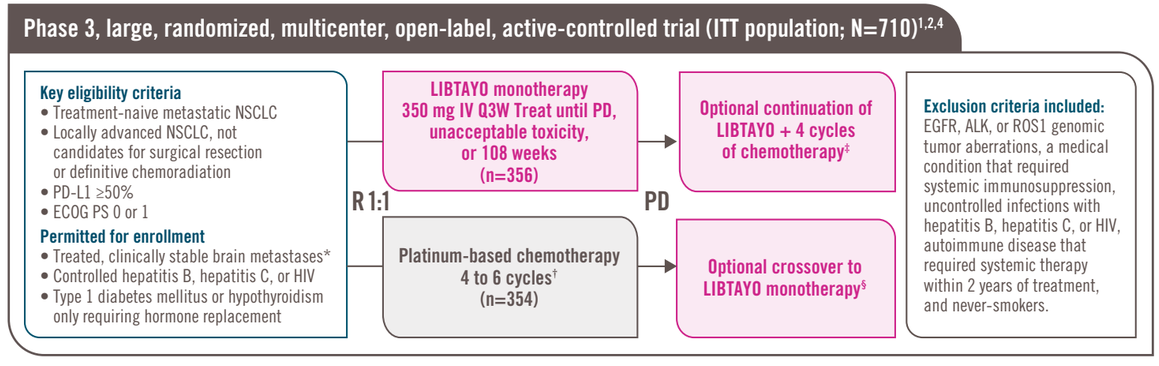
No dose reduction for LIBTAYO is recommended. In general, withhold LIBTAYO for severe (Grade 3) immune-mediated adverse reactions. Permanently discontinue LIBTAYO for life-threatening (Grade 4) immune-mediated adverse reactions, recurrent severe (Grade 3) immune-mediated adverse reactions that require systemic immunosuppressive treatment, or an inability to reduce corticosteroid dose to 10 mg or less of prednisone equivalent per day within 12 weeks of initiating steroids.

Withhold or permanently discontinue LIBTAYO depending on severity. In general, if LIBTAYO requires interruption or discontinuation, administer systemic corticosteroid therapy (1 to 2 mg/kg/day prednisone or equivalent) until improvement to Grade 1 or less. Upon improvement to Grade 1 or less, initiate corticosteroid taper and continue to taper over at least 1 month. Consider administration of other systemic immunosuppressants in patients whose immune-mediated adverse reactions are not controlled with corticosteroids.

Immune-mediated pneumonitis: LIBTAYO can cause immune-mediated pneumonitis. In patients treated with other PD-1/PD-L1–blocking antibodies, the incidence of pneumonitis is higher in patients who have received prior thoracic radiation. Immune-mediated pneumonitis occurred in 3.2% (26/810) of patients receiving LIBTAYO, including Grade 4 (0.5%), Grade 3 (0.5%), and Grade 2 (2.1%). Pneumonitis led to permanent discontinuation in 1.4% of patients and withholding of LIBTAYO in 2.1% of patients. Systemic corticosteroids were required in all patients with pneumonitis. Pneumonitis resolved in 58% of the 26 patients. Of the 17 patients in whom LIBTAYO was withheld, 9 reinitiated after symptom improvement; of these, 3/9 (33%) had recurrence of pneumonitis. Withhold LIBTAYO for Grade 2, and permanently discontinue for Grade 3 or 4. Resume in patients with complete or partial resolution (Grade 0 to 1) after corticosteroid taper. Permanently discontinue if no complete or partial resolution within 12 weeks of initiating

In patients who had no EGFR, ALK, or ROS1 aberrations:

EMPOWER-Lung 1 was designed to enroll advanced NSCLC patients with PD-L1 ≥50%[1]



The EMPOWER-Lung 1 study was designed to enroll patients with PD-L1 ≥50%.[2]

- A total of 710 patients were enrolled and randomized. For some patients, it was later determined that PD-L1 biomarker testing was not conducted according to the instructions for use, and required retesting[2]
- An analysis was conducted in a subset of patients with known PD-L1 ≥50% (n=563). The analysis excluded 91 patients from the overall population whose PD-L1 status was unknown because their tumors could not be retested, and 56 patients from the overall population who had <50% PD-L1 expression[2] (LIBTAYO is not indicated in patients with <50% PD-L1 expression)

Primary endpoints[1]:
- OS and PFS

Secondary endpoints included[1,2]:
- ORR (key), DOR, and safety and tolerability

Per IDMC recommendation:
Trial stopped early due to superior OS.[2]

LIBTAYO was examined in a clinical study that included historically underrepresented patients with advanced NSCLC[1,2]:

In the LIBTAYO arm (ITT patient population) at baseline, 12% of patients had treated and clinically stable brain metastases,* 18% had locally advanced disease, and 2% had controlled hepatitis B or hepatitis C. Patients with HIV were permitted to enroll, but none were recruited.[1,2,6]

The recommended dosage of LIBTAYO is 350 mg administered as an intravenous infusion over 30 minutes every 3 weeks until disease progression or unacceptable toxicity.[1]

*Patients were eligible if they had been adequately treated and had neurologically returned to baseline for at least 2 weeks prior to randomization.[1]

†Investigator's choice: Paclitaxel + cisplatin or carboplatin; gemcitabine + cisplatin or carboplatin; or pemetrexed + cisplatin or carboplatin followed by optional pemetrexed maintenance in patients with nonsquamous histology.[1]

‡Patients who experienced IRC-assessed RECIST 1.1-defined progressive disease on therapy with LIBTAYO were permitted to continue treatment with LIBTAYO 350 mg Q3W for up to 108 additional weeks, along with the addition of histology-specific chemotherapy for 4 cycles until further disease progression was observed.[1]

§Patients who experienced IRC-assessed RECIST 1.1-defined progressive disease on chemotherapy were permitted to receive treatment with LIBTAYO for up to 108 weeks.[1,4]

Randomization was stratified by histology (nonsquamous vs squamous) and geographic region (Europe vs Asia vs rest of world).[1]

Median duration of exposure was 27.3 weeks (range, 9 days-115 weeks) for LIBTAYO vs 17.7 weeks (range, 18 days-86.7 weeks) for chemotherapy.[1]

DOR=duration of response; ECOG=Eastern Cooperative Oncology Group; IDMC=independent data monitoring committee; IRC=independent review committee; IV=intravenous; ORR=objective response rate; PD=progressive disease; PFS=progression-free survival; PS=performance status; Q3W=every 3 weeks; R=randomization; RECIST=Response Evaluation Criteria in Solid Tumors.

Important Safety Information (continued)

Warnings and Precautions (continued)

Severe and Fatal Immune-Mediated Adverse Reactions (continued)

Immune-mediated pneumonitis (continued): steroids or inability to reduce prednisone to less than 10 mg per day (or equivalent) within 12 weeks of initiating steroids.

Immune-mediated colitis: LIBTAYO can cause immune-mediated colitis. The primary component of immune-mediated colitis was diarrhea.

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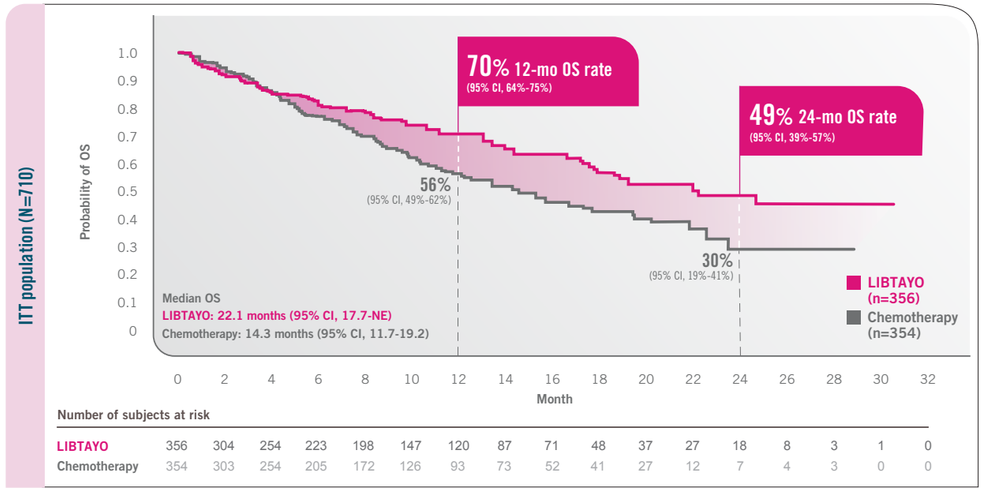
LIBTAYO® (cemiplimab-rwlc) Injection 350 mg

Approved in patients with advanced NSCLC* who had PD-L1 ≥50% and no EGFR, ALK, or ROS1 aberrations[1]

LIBTAYO significantly EXTENDED SURVIVAL vs platinum-based chemotherapy in EMPOWER-Lung 1[1,4]



32%
Reduction in risk of death HR=0.68

(95% CI, 0.53-0.87)
P=0.0022

Median OS: 22.1 months (95% CI, 17.7-NE) with LIBTAYO vs 14.3 months (95% CI, 11.7-19.2) with chemotherapy[1]

- Number of deaths: 30% of patients (108 out of 356 patients) with LIBTAYO and 40% of patients (141 out of 354 patients) with chemotherapy[1]
- **Nearly 3 out of 4 patients (74%)** who progressed on platinum-based chemotherapy crossed over to LIBTAYO treatment[1]

***Patients with locally advanced NSCLC who are not candidates for surgical resection or definitive chemoradiation or who have metastatic NSCLC.[1]**

Important Safety Information (continued)

Warnings and Precautions (continued)

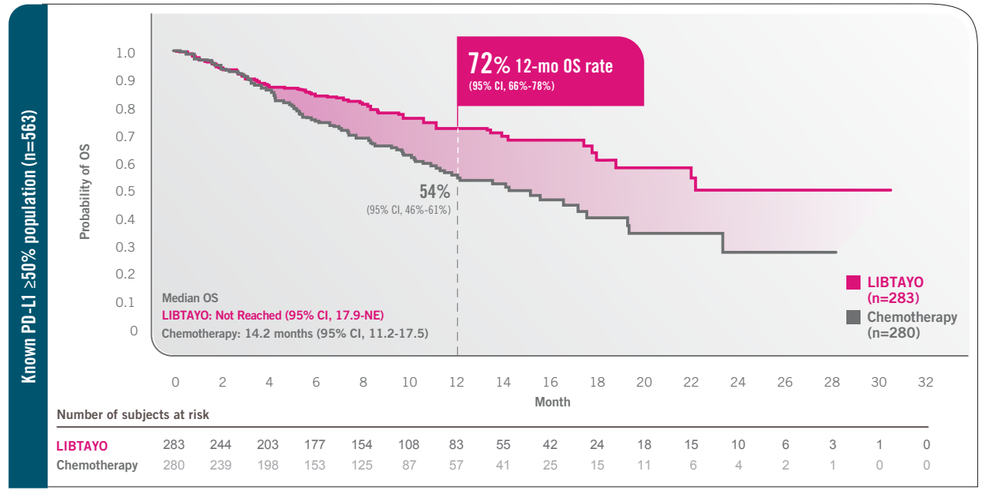
Severe and Fatal Immune-Mediated Adverse Reactions (continued)

Immune-mediated colitis (continued): Cytomegalovirus (CMV) infection/reactivation has been reported in patients with corticosteroid-refractory immune-mediated colitis treated with PD-1/PD-L1–blocking antibodies. In cases of corticosteroid-refractory immune-mediated colitis, consider repeating infectious workup to exclude alternative etiologies. Immune-mediated colitis occurred in 2.2% (18/810) of patients receiving LIBTAYO, including Grade 3 (0.9%) and Grade 2 (1.1%). Colitis led to permanent discontinuation in 0.4% of patients and withholding of LIBTAYO in 1.5% of patients. Systemic corticosteroids were required in all patients with colitis. Colitis resolved in 39% of the 18 patients. Of the 12 patients in whom LIBTAYO was withheld, 4 reinitiated LIBTAYO after symptom improvement; of these, 3/4 (75%) had recurrence. Withhold LIBTAYO for Grade 2 or 3, and permanently discontinue for Grade 4. Resume in patients with complete or partial resolution (Grade 0 to 1) after corticosteroid taper. Permanently discontinue if no complete or partial resolution within 12 weeks of initiating steroids or inability to reduce prednisone to less than 10 mg per day (or equivalent) within 12 weeks of initiating steroids.

Immune-mediated hepatitis: LIBTAYO can cause immune-mediated hepatitis. Immune-mediated hepatitis occurred in 2% (16/810) of patients receiving LIBTAYO, including fatal (0.1%), Grade 4 (0.1%), Grade 3 (1.4%), and Grade 2 (0.2%). Hepatitis led to permanent discontinuation of LIBTAYO in 1.2% of patients and withholding of LIBTAYO in 0.5% of patients. Systemic corticosteroids were required in all patients with hepatitis. Additional immunosuppression with mycophenolate was required in 19% (3/16) of these patients. Hepatitis resolved in 50% of the 16 patients. Of the 5 patients in whom LIBTAYO was withheld, 3 reinitiated LIBTAYO after symptom improvement; of these, none had recurrence.

In an analysis of the subset of patients with advanced NSCLC* who had no EGFR, ALK, or ROS1 aberrations and known PD-L1 ≥50% (n=563):

Overall survival with LIBTAYO vs platinum-based chemotherapy in EMPOWER-Lung 1[2-4]



43%
Reduction in risk of death HR=0.57

(95% CI, 0.42-0.77)
P=0.0002

Adapted with permission from Sezer et al, *Lancet* 2021.[2]

Median OS: Not Reached (95% CI, 17.9-NE) with LIBTAYO vs 14.2 months (95% CI, 11.2-17.5) with chemotherapy[2,3]

- Number of deaths: 25% of patients (70 out of 283 patients) with LIBTAYO and 38% of patients (105 out of 280 patients) with chemotherapy[2,3]
- **72% of patients** who progressed on platinum-based chemotherapy crossed over to LIBTAYO treatment[6]

***Patients with locally advanced NSCLC who were not candidates for surgical resection or definitive chemoradiation or who had metastatic NSCLC.[2]**

Important Safety Information (continued)

Warnings and Precautions (continued)

Severe and Fatal Immune-Mediated Adverse Reactions (continued)

Immune-mediated hepatitis (continued):

For hepatitis with no tumor involvement of the liver: Withhold LIBTAYO if AST or ALT increases to more than 3 and up to 8 times the upper limit of normal (ULN) or if total bilirubin increases to more than 1.5 and up to 3 times the ULN. Permanently discontinue LIBTAYO if AST or ALT increases to more than 8 times the ULN or total bilirubin increases to more than 3 times the ULN.

For hepatitis with tumor involvement of the liver: Withhold LIBTAYO if baseline AST or ALT is more than 1 and up to 3 times ULN and increases to more than 5 and up to 10 times ULN. Also, withhold LIBTAYO if baseline AST or ALT is more than 3 and up to 5 times ULN and increases to more than 8 and up to 10 times ULN. Permanently discontinue LIBTAYO if AST or ALT increases to more than 10 times ULN or if total bilirubin increases to more than 3 times ULN. If AST and ALT are less than or equal to ULN at baseline, withhold or permanently discontinue LIBTAYO based on recommendations for hepatitis with no liver involvement.

Resume in patients with complete or partial resolution (Grade 0 to 1) after corticosteroid taper. Permanently discontinue if no complete or partial resolution within 12 weeks of initiating steroids or inability to reduce prednisone to less than 10 mg per day (or equivalent) within 12 weeks of initiating steroids.

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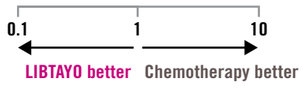
Approved in patients with advanced NSCLC* with PD-L1 ≥50% and no EGFR, ALK, or ROS1 aberrations[1]

Analysis of overall survival by subgroups[4]

ITT population (N=710)

	Events, n (total) LIBTAYO	Events, n (total) Chemotherapy	HR (95% CI)
Overall	108 (356)	141 (354)	0.68 (0.53-0.87)
Age			
<65 years	61 (200)	71 (190)	0.72 (0.51-1.02)
≥65 years	47 (156)	70 (164)	0.63 (0.43-0.91)
Sex			
Male	93 (312)	123 (294)	0.64 (0.49-0.84)
Female	15 (44)	18 (60)	0.87 (0.42-1.78)
Region of enrollment			
Europe	85 (275)	119 (278)	0.62 (0.47-0.82)
Asia	10 (39)	8 (38)	1.34 (0.52-3.42)
Rest of the world	13 (42)	14 (38)	0.73 (0.34-1.56)
ECOG PS			
0	25 (96)	32 (96)	0.78 (0.46-1.32)
1	83 (260)	109 (258)	0.66 (0.49-0.88)
Histology			
Squamous	45 (159)	65 (152)	0.53 (0.36-0.77)
Nonsquamous	63 (197)	76 (202)	0.83 (0.59-1.16)
Brain metastases at baseline			
Yes	9 (44)	15 (39)	0.44 (0.19-1.07)
No	99 (312)	126 (315)	0.71 (0.54-0.92)
Cancer stage at screening			
Locally advanced	17 (63)	16 (52)	0.85 (0.43-1.68)
Metastatic	91 (293)	125 (302)	0.68 (0.52-0.89)



Adapted with permission from Sezer et al, *Lancet* 2021 supplementary appendix.[4]

*Patients with locally advanced NSCLC who are not candidates for surgical resection or definitive chemoradiation or who have metastatic NSCLC.[1]

Limitations:
OS subgroup analyses were not powered to show a statistically significant difference between or within individual subgroups. Furthermore, histology, brain metastases at baseline, and cancer stage at screening were not prespecified subgroup analyses. Firm conclusions cannot be made based on these subgroup analyses.

Important Safety Information (continued)

Warnings and Precautions (continued)

Severe and Fatal Immune-Mediated Adverse Reactions (continued)

Immune-mediated endocrinopathies: For Grade 3 or 4 endocrinopathies, withhold until clinically stable or permanently discontinue depending on severity.

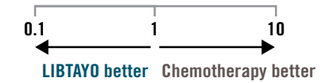
- **Adrenal insufficiency:** LIBTAYO can cause primary or secondary adrenal insufficiency. For Grade 2 or higher adrenal insufficiency, initiate symptomatic treatment, including hormone replacement as clinically indicated. Withhold LIBTAYO depending on severity.

In an analysis of the subset of patients with advanced NSCLC* who had no EGFR, ALK, or ROS1 aberrations and known PD-L1 ≥50% (n=563):

Post hoc analysis of overall survival by subgroups[2]

Known PD-L1 ≥50% population (n=563)

	Events, n (total) LIBTAYO	Events, n (total) Chemotherapy	HR (95% CI)
Overall	70 (283)	105 (280)	0.57 (0.42-0.77)
Age			
<65 years	41 (157)	50 (147)	0.66 (0.44-1.00)
≥65 years	29 (126)	55 (133)	0.48 (0.30-0.76)
Sex			
Male	58 (248)	92 (231)	0.50 (0.36-0.69)
Female	12 (35)	13 (49)	1.11 (0.49-2.52)
Region of enrollment			
Europe	55 (215)	84 (216)	0.54 (0.39-0.77)
Asia	5 (31)	7 (29)	0.76 (0.24-2.41)
Rest of the world	10 (37)	14 (35)	0.59 (0.26-1.33)
ECOG PS			
0	18 (77)	23 (75)	0.77 (0.41-1.44)
1	52 (206)	82 (205)	0.54 (0.38-0.76)
Histology			
Squamous	30 (122)	48 (121)	0.48 (0.30-0.77)
Nonsquamous	40 (161)	57 (159)	0.64 (0.43-0.96)
Brain metastases at baseline			
Yes	4 (34)	12 (34)	0.17 (0.04-0.76)
No	66 (249)	93 (246)	0.60 (0.44-0.83)
Cancer stage at screening			
Locally advanced	9 (45)	15 (42)	0.48 (0.20-1.14)
Metastatic	61 (238)	90 (238)	0.59 (0.43-0.82)



Adapted with permission from Sezer et al, *Lancet* 2021.[2]

*Patients with locally advanced NSCLC who were not candidates for surgical resection or definitive chemoradiation or who had metastatic NSCLC.[2]

Limitations:
OS subgroup analyses were not powered to show a statistically significant difference between or within individual subgroups. Furthermore, none of the subgroup analyses were prespecified in the subset of patients with known PD-L1 ≥50%. Firm conclusions cannot be made based on these subgroup analyses.

Important Safety Information (continued)

Warnings and Precautions (continued)

Severe and Fatal Immune-Mediated Adverse Reactions (continued)

Immune-mediated endocrinopathies (continued):

- **Adrenal insufficiency (continued):** Adrenal insufficiency occurred in 0.4% (3/810) of patients receiving LIBTAYO, including Grade 3 (0.4%). Adrenal insufficiency led to permanent discontinuation of LIBTAYO in 1 (0.1%) patient. LIBTAYO was not withheld in

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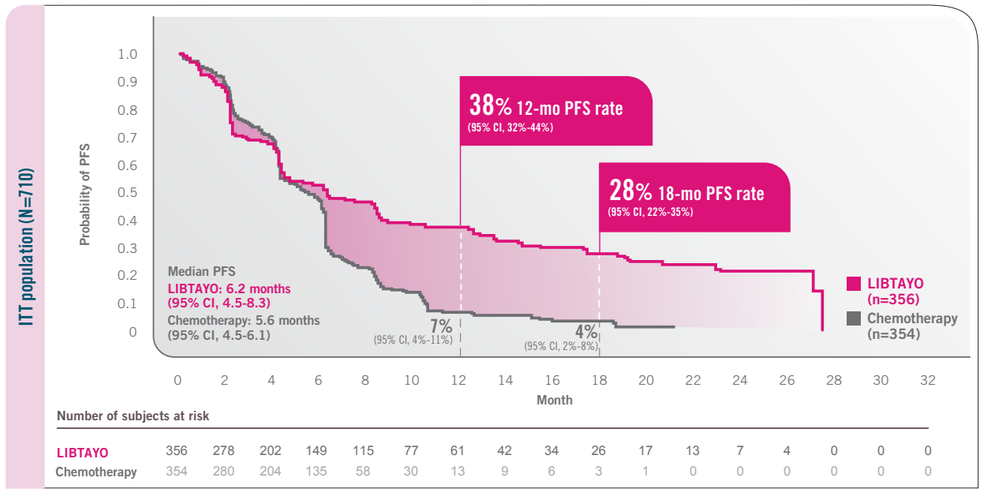
Approved in patients with advanced NSCLC* who had PD-L1 ≥50% and no EGFR, ALK, or ROS1 aberrations[1]

LIBTAYO significantly EXTENDED PROGRESSION-FREE SURVIVAL† vs platinum-based chemotherapy in EMPOWER-Lung 1[1,4]



41%
Reduction in risk of progressive disease HR=0.59

(95% CI, 0.49-0.72)
P<0.0001

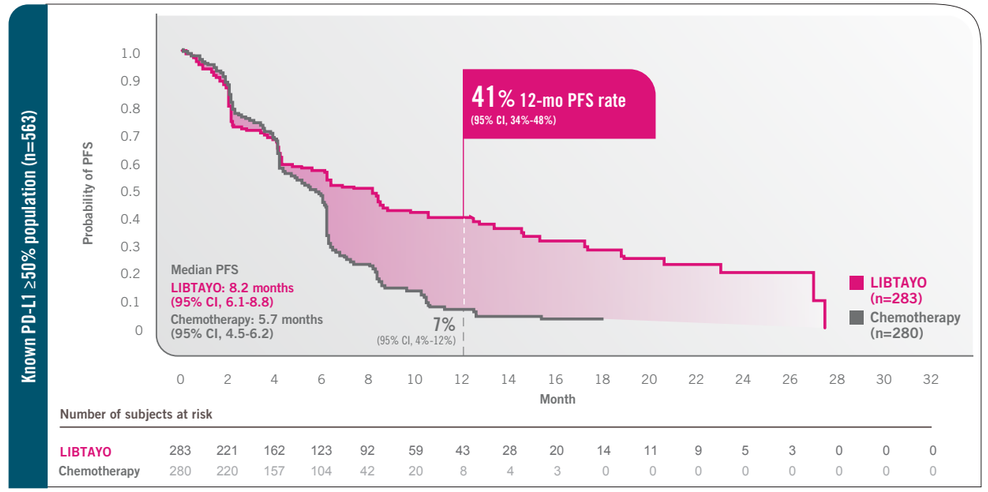
Adapted with permission from Sezer et al, *Lancet* supplementary appendix.[4]

- **Median PFS: 6.2 months** (95% CI, 4.5-8.3) with LIBTAYO vs 5.6 months (95% CI, 4.5-6.1) with chemotherapy[1]
- Number of events: 57% of patients (201 out of 356 patients) with LIBTAYO and 74% of patients (262 out of 354 patients) with chemotherapy[1]
- Overall response rate†‡: 37% (95% CI, 32%-42%) (CR=3%, PR=33%) with LIBTAYO vs 21% (95% CI, 17%-25%) (CR=1%, PR=20%) with chemotherapy[1]
- Duration of response†: Median of 21 months (range, 1.9+-23.3+ months) with LIBTAYO vs 6 months (range, 1.3+-16.5+ months) with chemotherapy[1]

***Patients with locally advanced NSCLC who are not candidates for surgical resection or definitive chemoradiation or who have metastatic NSCLC.[1]**
†Per BICR.[1]
‡Clopper-Pearson exact confidence interval.[1]
+: Ongoing response.[1]

In an analysis of the subset of patients with advanced NSCLC* who had no EGFR, ALK, or ROS1 aberrations and known PD-L1 ≥50% (n=563):

Progression-free survival† with LIBTAYO vs platinum-based chemotherapy in EMPOWER-Lung 1[2,3]



46%
Reduction in risk of progressive disease HR=0.54

(95% CI, 0.43-0.68)
P<0.0001

Adapted with permission from Sezer et al, *Lancet* 2021.[2]

- **Median PFS: 8.2 months** (95% CI, 6.1-8.8) with LIBTAYO vs 5.7 months (95% CI, 4.5-6.2) with chemotherapy[2,3]
- Number of events: 52% of patients (147 out of 283 patients) with LIBTAYO and 70% of patients (197 out of 280 patients) with chemotherapy[2,3]
- Overall response rate†‡§: 39% (95% CI, 34%-45%) (CR=2%, PR=37%) with LIBTAYO vs 20% (95% CI, 16%-26%) (CR=1%, PR=19%) with chemotherapy[2,3]
- Duration of response†§: Median of 16.7 months (range, 1.9+-23.3+ months) with LIBTAYO vs 6 months (range, 1.3+-14.5+ months) with chemotherapy[2,3]

***Patients with locally advanced NSCLC who were not candidates for surgical resection or definitive chemoradiation or who had metastatic NSCLC.[2]**
†Per BICR.[2,3]
‡Clopper-Pearson exact confidence interval.[2,3]
§Not a prespecified endpoint in the 563-patient population with known PD-L1 ≥50%.[6]
+: Ongoing response.[3]

Important Safety Information (continued)

Warnings and Precautions (continued)

Severe and Fatal Immune-Mediated Adverse Reactions (continued)

Immune-mediated endocrinopathies (continued):

- **Adrenal insufficiency (continued):** any patient due to adrenal insufficiency. Systemic corticosteroids were required in all patients with adrenal insufficiency; of these, 67% (2/3) remained on systemic corticosteroids. Adrenal insufficiency had not resolved in any patient at the time of data cutoff
- **Hypophysitis:** LIBTAYO can cause immune-mediated hypophysitis. Hypophysitis can present with acute symptoms associated with mass effect such as headache, photophobia, or visual field defects. Hypophysitis can cause hypopituitarism. Initiate hormone replacement as clinically indicated. Withhold or permanently discontinue

Important Safety Information (continued)

Warnings and Precautions (continued)

Severe and Fatal Immune-Mediated Adverse Reactions (continued)

Immune-mediated endocrinopathies (continued):

- **Hypophysitis (continued):** depending on severity. Hypophysitis occurred in 0.4% (3/810) of patients receiving LIBTAYO, including Grade 3 (0.2%) and Grade 2 (0.1%) adverse reactions. Hypophysitis led to permanent discontinuation of LIBTAYO in 1 (0.1%) patient and withholding of LIBTAYO in 1 (0.1%) patient. Systemic corticosteroids were required in 67% (2/3) of patients with hypophysitis. Hypophysitis had not resolved in any patient at the time of data cutoff

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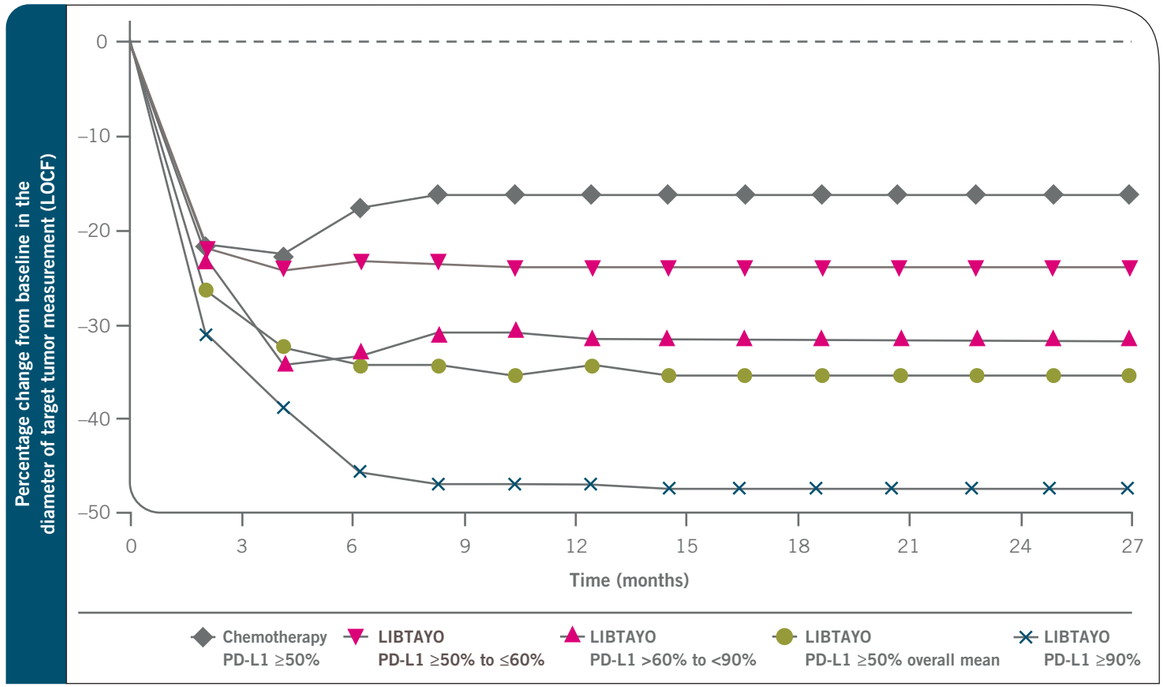
In the subset of patients with advanced NSCLC* with no EGFR, ALK, or ROS1 aberrations and known PD-L1 ≥50% (n=563):

Exploratory analysis of PD-L1 expression[2]

Change in target tumor measurement with baseline PD-L1 tumor proportion scores[2]



Adapted with permission from Sezer et al, *Lancet* 2021.[2]

***Patients with locally advanced NSCLC who were not candidates for surgical resection or definitive chemoradiation or who had metastatic NSCLC.[2]**

LOCF=last observation carried forward.

Limitations:
This is an exploratory analysis that was not powered to show a statistically significant difference between or within varying PD-L1 expression levels. Firm conclusions cannot be made based on these exploratory analyses.

Important Safety Information (continued)

Warnings and Precautions (continued)

Severe and Fatal Immune-Mediated Adverse Reactions (continued)

Immune-mediated endocrinopathies (continued):

- **Thyroid disorders:** LIBTAYO can cause immune-mediated thyroid disorders. Thyroiditis can present with or without endocrinopathy. Hypothyroidism can follow hyperthyroidism. Initiate hormone replacement or medical management of hyperthyroidism as clinically indicated. Withhold or permanently discontinue LIBTAYO depending on severity
- **Thyroiditis:** Thyroiditis occurred in 0.6% (5/810) of patients receiving LIBTAYO, including Grade 2 (0.2%) adverse reactions. No patient discontinued LIBTAYO due to thyroiditis. Thyroiditis led to withholding of LIBTAYO in 1 patient. Systemic corticosteroids were not required in any patient with thyroiditis. Thyroiditis had not resolved in any patient at the time of data cutoff. Blood thyroid stimulating hormone increased and blood thyroid stimulating hormone decreased have also been reported
- **Hyperthyroidism:** Hyperthyroidism occurred in 3.2% (26/810) of patients receiving LIBTAYO, including Grade 2 (0.9%). No patient discontinued treatment and LIBTAYO was withheld in 0.5% of patients due to hyperthyroidism. Systemic corticosteroids were required in 3.8% (1/26) of patients. Hyperthyroidism resolved in 50% of 26 patients. Of the 4 patients in whom LIBTAYO was withheld for hyperthyroidism, 2 patients reinitiated LIBTAYO after symptom improvement; of these, none had recurrence of hyperthyroidism

In the subset of patients with advanced NSCLC* with no EGFR, ALK, or ROS1 aberrations and known PD-L1 ≥50% (n=563):

Exploratory analysis of PD-L1 expression[2]

Overall survival and objective response with measurement with baseline PD-L1 tumor proportion scores[2]

	PD-L1 ≥90%		PD-L1 >60% to <90%		PD-L1 ≥50% to ≤60%	
Number of patients	**LIBTAYO (n=98)**	**Chemotherapy (n=94)**	**LIBTAYO (n=89)**	**Chemotherapy (n=90)**	**LIBTAYO (n=96)**	**Chemotherapy (n=96)**
Overall survival						
Median, months (95% CI)	NR (17.3-NE)	15.1 (11.1-NE)	22.1 (17.9-NE)	12.0 (9.6-19.2)	21.9 (13.2-NE)	14.0 (9.4-19.3)
Hazard ratio (95% CI)	0.46 (0.25-0.85)		0.47 (0.27-0.80)		0.77 (0.49-1.23)	
Progression-free survival						
Median, months (95% CI)	15.3 (10.4-18.7)	5.9 (4.3-6.2)	6.2 (4.2-8.4)	4.2 (4.1-5.7)	4.3 (2.8-6.3)	6.2 (5.0-6.2)
Hazard ratio (95% CI)	0.28 (0.17-0.46)		0.55 (0.38-0.80)		0.79 (0.56-1.12)	
Tumor response						
Objective response rate, % (95% CI)	46 (36-56)	18 (11-27)	39 (29-50)	20 (12-30)	32 (23-43)	23 (15-33)

Adapted with permission from Sezer et al, *Lancet* 2021.[2]

***Patients with locally advanced NSCLC who were not candidates for surgical resection or definitive chemoradiation or who had metastatic NSCLC.[2]**

Limitations:
This is an exploratory analysis that was not powered to show a statistically significant difference between or within varying PD-L1 expression levels. Firm conclusions cannot be made based on these exploratory analyses.

Important Safety Information (continued)

Warnings and Precautions (continued)

Severe and Fatal Immune-Mediated Adverse Reactions (continued)

Immune-mediated endocrinopathies (continued):

- **Hypothyroidism:** Hypothyroidism occurred in 7% (60/810) of patients receiving LIBTAYO, including Grade 2 (6%). Hypothyroidism led to permanent discontinuation of LIBTAYO in 1 (0.1%) patient. Hypothyroidism led to withholding of LIBTAYO in 1.1% of patients. Systemic corticosteroids were not required in any patient with hypothyroidism. Hypothyroidism resolved in 8.3% of the 60 patients. Majority of the patients with hypothyroidism required long-term thyroid hormone replacement. Of the 9 patients in whom LIBTAYO was withheld for hypothyroidism, 1 reinitiated LIBTAYO after symptom improvement; 1 required ongoing hormone replacement therapy
- **Type 1 diabetes mellitus, which can present with diabetic ketoacidosis:** Monitor for hyperglycemia or other signs and symptoms of diabetes. Initiate treatment with insulin as clinically indicated. Withhold LIBTAYO depending on severity. Type 1 diabetes mellitus occurred in 0.1% (1/810) of patients, including Grade 4 (0.1%). No patient discontinued treatment due to type 1 diabetes mellitus. Type 1 diabetes mellitus led to withholding of LIBTAYO in 0.1% of patients

Please see additional Important Safety Information throughout and click here for full Prescribing Information.

LIBTAYO® (cemiplimab-rwlc) Injection 350 mg

LIBTAYO demonstrated a favorable safety profile in EMPOWER-Lung 1[1]

Adverse reactions in ≥10% of patients[1]

Adverse reactions	LIBTAYO (n=355)		Chemotherapy (n=342)	
	All Grades, %	Grade 3-4, %	All Grades, %	Grade 3-4, %
Musculoskeletal and connective tissue disorders				
Musculoskeletal pain*	26	0.6	27	1.5
Skin and subcutaneous tissue disorders				
Rash†	15	1.4	6	0
Blood and lymphatic system disorders				
Anemia	15	3.4	50	16
General disorders and administration site conditions				
Fatigue‡	14	1.1	26	2
Metabolism and nutrition disorders				
Decreased appetite	12	0.6	18	0.3
Infections and infestations				
Pneumonia§	11	5	12	5
Respiratory, thoracic, and mediastinal disorders				
Cough‖	11	0	8	0.3

*Musculoskeletal pain is a composite term that includes back pain, arthralgia, pain in extremity, musculoskeletal pain, musculoskeletal chest pain, bone pain, myalgia, neck pain, spinal pain, and musculoskeletal stiffness.
†Rash is a composite term that includes rash, dermatitis, urticaria, rash maculopapular, erythema, rash erythematous, rash pruritic, psoriasis, autoimmune dermatitis, dermatitis acneiform, dermatitis allergic, dermatitis atopic, dermatitis bullous, drug eruption, dyshidrotic eczema, lichen planus, and skin reaction.
‡Fatigue is a composite term that includes fatigue, asthenia, and malaise.
§Pneumonia is a composite term that includes atypical pneumonia, embolic pneumonia, lower respiratory tract infection, lung abscess, paracancerous pneumonia, pneumonia, pneumonia bacterial, and pneumonia klebsiella.
‖Cough is a composite term that includes cough and productive cough.
Toxicity was graded per National Cancer Institute Common Terminology Criteria for Adverse Events (NCI CTCAE) v4.03.
HSCT=hematopoietic stem cell transplantation.

- LIBTAYO was permanently discontinued due to adverse reactions in 6% of patients[1];
- Adverse reactions resulting in permanent discontinuation in at least 2 patients were pneumonitis, pneumonia, ischemic stroke, and increased aspartate aminotransferase[1]
- Serious adverse reactions occurred in 28% of patients receiving LIBTAYO[1];
- The most frequent serious adverse reactions in at least 2% of patients were pneumonia and pneumonitis[1]

Warnings and Precautions for LIBTAYO[1]

Warnings and Precautions for LIBTAYO include severe and fatal immune-mediated adverse reactions such as immune-mediated pneumonitis, immune-mediated colitis, immune-mediated hepatitis, immune-mediated endocrinopathies, immune-mediated nephritis with renal dysfunction, immune-mediated dermatologic adverse reactions, and other immune-mediated adverse reactions; infusion-related reactions; complications of allogeneic HSCT; and embryo-fetal toxicity. Monitor for symptoms and signs of immune-mediated adverse reactions.

For more information on Warnings and Precautions, see additional Important Safety Information throughout and in Section 5 of the full Prescribing Information.

LIBTAYO safety profile in EMPOWER-Lung 1[1]

Grade 3 or 4 laboratory abnormalities worsening from baseline in ≥1% of patients[1]

Laboratory abnormalities	LIBTAYO (n=355)	Chemotherapy (n=342)
	Grade 3-4, %*	
Chemistry		
Increased aspartate aminotransferase	3.9	1.2
Increased alanine aminotransferase	2.7	0.3
Increased alkaline phosphatase	2.4	0.3
Increased blood bilirubin	2.1	0.3
Hypoalbuminemia	1.8	1.3
Increased creatinine	1.2	1.6
Hematology		
Lymphopenia	7	9
Anemia	2.7	16
Electrolytes		
Hyponatremia	6	7
Hyperkalemia	4.2	1.9
Hypocalcemia	3.9	3.4
Hypophosphatemia	2.4	4.1
Hypermagnesemia	2.1	1.6
Hypokalemia	1.5	2.2
Hypercalcemia	1.2	2.2

*Percentages are based on the number of patients with at least 1 postbaseline value available for that parameter.
Toxicity graded per NCI CTCAE v4.03.

Important Safety Information (continued)

Warnings and Precautions (continued)

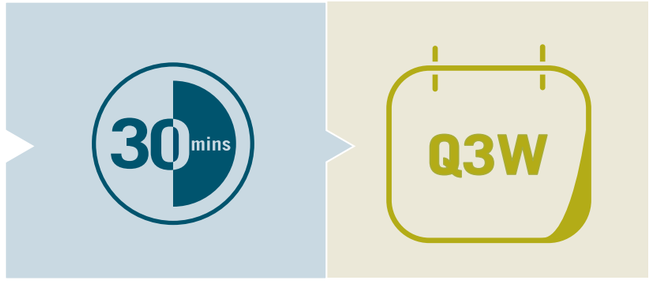
Severe and Fatal Immune-Mediated Adverse Reactions (continued)

Immune-mediated nephritis with renal dysfunction: LIBTAYO can cause immune-mediated nephritis. Immune-mediated nephritis occurred in 0.6% (5/810) of patients receiving LIBTAYO, including fatal (0.1%), Grade 3 (0.1%), and Grade 2 (0.4%). Nephritis led to permanent discontinuation in 0.1% of patients and withholding of LIBTAYO in 0.4% of patients. Systemic corticosteroids were required in all patients with nephritis. Nephritis resolved in 80% of the 5 patients. Of the 3 patients in whom LIBTAYO was withheld, 2 reinitiated LIBTAYO after symptom improvement; of these, none had recurrence. Withhold LIBTAYO for Grade 2 or 3 increased blood creatinine, and permanently discontinue for Grade 4 increased blood creatinine. Resume in patients with complete or partial resolution (Grade 0 to 1) after corticosteroid taper. Permanently discontinue if no complete or partial resolution within 12 weeks of initiating steroids or inability to reduce prednisone to less than 10 mg per day (or equivalent) within 12 weeks of initiating steroids.

Please see additional Important Safety Information throughout and click here for full Prescribing Information.

LIBTAYO® (cemiplimab-rwlc)
Injection 350 mg

LIBTAYO has straightforward dosing[1]



A fixed 350 mg dose from a single-dose vial

An IV infusion over 30 minutes

Every 3 weeks

Treatment should be continued until disease progression or unacceptable toxicity[1]

Important Safety Information (continued)

Warnings and Precautions (continued)

Severe and Fatal Immune-Mediated Adverse Reactions (continued)

Immune-mediated dermatologic adverse reactions: LIBTAYO can cause immune-mediated rash or dermatitis. Exfoliative dermatitis, including Stevens-Johnson syndrome (SJS), toxic epidermal necrolysis (TEN), and drug rash with eosinophilia and systemic symptoms (DRESS) has occurred with PD-1/PD-L1–blocking antibodies. Immune-mediated dermatologic adverse reactions occurred in 1.6% (13/810) of patients receiving LIBTAYO, including Grade 3 (0.9%) and Grade 2 (0.6%). Immune-mediated dermatologic adverse reactions led to permanent discontinuation in 0.1% of patients and withholding of LIBTAYO in 1.4% of patients. Systemic corticosteroids were required in all patients with immune-mediated dermatologic adverse reactions. Immune-mediated dermatologic adverse reactions resolved in 69% of the 13 patients. Of the 11 patients in whom LIBTAYO was withheld for dermatologic adverse reactions, 7 reinitiated LIBTAYO after symptom improvement; of these, 43% (3/7) had recurrence of the dermatologic adverse reaction. Topical emollients and/or topical corticosteroids may be adequate to treat mild to moderate non-exfoliative rashes. Withhold LIBTAYO for suspected SJS, TEN, or DRESS. Permanently discontinue LIBTAYO for confirmed SJS, TEN, or DRESS. Resume in patients with complete or partial resolution (Grade 0 to 1) after corticosteroid taper. Permanently discontinue if no complete or partial resolution within 12 weeks of initiating steroids or inability to reduce prednisone to less than 10 mg per day (or equivalent) within 12 weeks of initiating steroids.

Other immune-mediated adverse reactions: The following clinically significant immune-mediated adverse reactions occurred at an incidence of <1% in 810 patients who received LIBTAYO or were reported with the use of other PD-1/PD-L1–blocking antibodies. Severe or fatal cases have been reported for some of these adverse reactions.

- **Cardiac/vascular:** Myocarditis, pericarditis, and vasculitis. Permanently discontinue for Grades 2, 3, or 4 myocarditis
- **Nervous system:** Meningitis, encephalitis, myelitis and demyelination, myasthenic syndrome/myasthenia gravis (including exacerbation), Guillain-Barré syndrome, nerve paresis, and autoimmune neuropathy. Withhold for Grade 2 neurological toxicities and permanently discontinue for Grades 3 or 4 neurological toxicities. Resume in patients with complete or partial resolution (Grade 0 to 1) after corticosteroid taper. Permanently discontinue if no complete or partial resolution within 12 weeks of initiating steroids or inability to reduce prednisone to less than 10 mg per day (or equivalent) within 12 weeks of initiating steroids

Important Safety Information (continued)

Warnings and Precautions (continued)

Severe and Fatal Immune-Mediated Adverse Reactions (continued)

Other immune-mediated adverse reactions (continued):

- **Ocular:** Uveitis, iritis, and other ocular inflammatory toxicities. Some cases can be associated with retinal detachment. Various grades of visual impairment to include blindness can occur. If uveitis occurs in combination with other immune-mediated adverse reactions, consider a Vogt-Koyanagi-Harada–like syndrome, as this may require treatment with systemic steroids to reduce the risk of permanent vision loss
- **Gastrointestinal:** Pancreatitis to include increases in serum amylase and lipase levels, gastritis, duodenitis, stomatitis
- **Musculoskeletal and connective tissue:** Myositis/polymyositis, rhabdomyolysis, and associated sequelae including renal failure, arthritis, polymyalgia rheumatica
- **Endocrine:** Hypoparathyroidism
- **Other (hematologic/immune):** Hemolytic anemia, aplastic anemia, hemophagocytic lymphohistiocytosis, systemic inflammatory response syndrome, histiocytic necrotizing lymphadenitis (Kikuchi lymphadenitis), sarcoidosis, immune thrombocytopenic purpura, solid organ transplant rejection

Infusion-related reactions

Severe infusion-related reactions (Grade 3) occurred in 0.1% of patients receiving LIBTAYO as a single agent. Monitor patients for signs and symptoms of infusion-related reactions. The most common symptoms of infusion-related reaction were nausea, pyrexia, rash, and dyspnea. Interrupt or slow the rate of infusion for Grade 1 or 2, and permanently discontinue for Grade 3 or 4.

Complications of allogeneic HSCT

Fatal and other serious complications can occur in patients who receive allogeneic hematopoietic stem cell transplantation (HSCT) before or after being treated with a PD-1/PD-L1–blocking antibody. Transplant-related complications include hyperacute graft-versus-host disease (GVHD), acute GVHD, chronic GVHD, hepatic veno-occlusive disease (VOD) after reduced intensity conditioning, and steroid-requiring febrile syndrome (without an identified infectious cause). These complications may occur despite intervening therapy between PD-1/PD-L1 blockade and allogeneic HSCT. Follow patients closely for evidence of transplant-related complications and intervene promptly. Consider the benefit versus risks of treatment with a PD-1/PD-L1–blocking antibody prior to or after an allogeneic HSCT.

Embryo-fetal toxicity

LIBTAYO can cause fetal harm when administered to a pregnant woman due to an increased risk of immune-mediated rejection of the developing fetus resulting in fetal death. Advise women of the potential risk to a fetus. Advise females of reproductive potential to use effective contraception during treatment with LIBTAYO and for at least 4 months after the last dose.

Adverse Reactions

- In the pooled safety analysis of 810 patients, the most common adverse reactions (≥15%) with LIBTAYO were musculoskeletal pain, fatigue, rash, and diarrhea
- In the pooled safety analysis of 810 patients, the most common Grade 3-4 laboratory abnormalities (≥2%) with LIBTAYO were lymphopenia, hyponatremia, hypophosphatemia, increased aspartate aminotransferase, anemia, and hyperkalemia

Use in Specific Populations

- **Lactation:** Because of the potential for serious adverse reactions in breastfed children, advise women not to breastfeed during treatment and for at least 4 months after the last dose of LIBTAYO
- **Females and males of reproductive potential:** Verify pregnancy status in females of reproductive potential prior to initiating LIBTAYO

Please click here for full Prescribing Information.

References: 1. LIBTAYO (cemiplimab-rwlc) injection full U.S. prescribing information. Regeneron Pharmaceuticals, Inc., and sanofi-aventis U.S. LLC. **2.** Sezer A, Kilickap S, Gümüş M, et al. Cemiplimab monotherapy for first-line treatment of advanced non-small-cell lung cancer with PD-L1 of at least 50%: a multicentre, open-label, global, phase 3, randomised, controlled trial. *Lancet*. 2021;397(10274):592-604. **3.** PD-L1 IHC 22C3 pharmDx [instructions for use]. Carpinteria, CA: Dako, Agilent Pathology Solutions; 2021. **4.** Sezer A, Kilickap S, Gümüş M, et al. Cemiplimab monotherapy for first-line treatment of advanced non-small-cell lung cancer with PD-L1 of at least 50%: a multicentre, open-label, global, phase 3, randomised, controlled trial. *Lancet.* 2021;397(10274) (suppl):1-178. **5.** Referenced with permission from the *NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Non-Small Cell Lung Cancer V.5.2021.* © National Comprehensive Cancer Network, Inc. 2021. All rights reserved. Accessed June 16, 2021. To view the most recent and complete version of the guidelines, go online to NCCN.org. **6.** Data on file. Regeneron Pharmaceuticals, Inc.

LIBTAYO®
(cemiplimab-rwlc)
Injection 350 mg

Overall survival with LIBTAYO vs platinum-based chemotherapy in EMPOWER-Lung 1[1-3]*

Overall survival

ITT patient population (N=710)[1]

Median OS: 22.1 months (95% CI, 17.7-NE) vs 14.3 months (95% CI, 11.7-19.2) (chemotherapy†), HR=0.68, *P*=0.0022[1]

32% reduction in risk of death; HR=0.68, *P*=0.0022[1]

Number of deaths: 30% of patients (108 out of 356 patients) with LIBTAYO and 40% of patients (141 out of 354 patients) with chemotherapy[1]

Nearly 3 out of 4 patients (74%) crossed over from chemotherapy to LIBTAYO treatment[1]

The EMPOWER-Lung 1 study was designed to enroll patients with PD-L1 ≥50%.[2]

- A total of 710 patients were enrolled and randomized. For some patients, it was later determined that PD-L1 biomarker testing was not conducted according to the instructions for use, and required retesting[2]
- An analysis was conducted in a subset of patients with known PD-L1 ≥50% (n=563). The analysis excluded 91 patients from the overall population whose PD-L1 status was unknown because their tumors could not be retested, and 56 patients from the overall population who had <50% PD-L1 expression[2] (LIBTAYO is not indicated in patients with <50% PD-L1 expression)

Known PD-L1 ≥50% patient population (n=563)[2,3]

Median OS: NR (95% CI, 17.9-NE) vs 14.2 months (95% CI, 11.2-17.5) (chemotherapy†), HR=0.57, *P*=0.0002[2,3]

43% reduction in risk of death; HR=0.57, *P*=0.0002[2,3]

Number of deaths: 25% of patients (70 out of 283 patients) with LIBTAYO and 38% of patients (105 out of 280 patients) with chemotherapy[2,3]

72% of patients crossed over from chemotherapy to LIBTAYO treatment[6]

Safety profile

In EMPOWER-Lung 1[1]

- LIBTAYO was permanently discontinued due to adverse reactions in 6% of patients[1];
- Adverse reactions resulting in permanent discontinuation in at least 2 patients were pneumonitis, pneumonia, ischemic stroke, and increased aspartate aminotransferase[1]
- Serious adverse reactions occurred in 28% of patients receiving LIBTAYO[1];
- The most frequent serious adverse reactions in at least 2% of patients were pneumonia and pneumonitis[1]

Enrollment

EMPOWER-Lung 1 included historically underrepresented patients[1,2]:

In the LIBTAYO arm (ITT patient population) at baseline: Treated and clinically stable brain metastases (12%), locally advanced disease (18%), and controlled infections with hepatitis B or hepatitis C (2%).[1,2,6]

*Investigator's choice: Paclitaxel + cisplatin or carboplatin; gemcitabine + cisplatin or carboplatin; or pemetrexed + cisplatin or carboplatin followed by optional pemetrexed maintenance in patients with nonsquamous histology.[1-4]

†Platinum-based.[1-3]

Warnings and Precautions for LIBTAYO[1]

Warnings and Precautions for LIBTAYO include severe and fatal immune-mediated adverse reactions such as immune-mediated pneumonitis, immune-mediated colitis, immune-mediated hepatitis, immune-mediated endocrinopathies, immune-mediated nephritis with renal dysfunction, immune-mediated dermatologic adverse reactions, and other immune-mediated adverse reactions; infusion-related reactions; complications of allogeneic HSCT; and embryo-fetal toxicity. Monitor for symptoms and signs of immune-mediated adverse reactions.

For more information on Warnings and Precautions, see additional Important Safety Information throughout and in Section 5 of the full Prescribing Information.

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