Gemeinsamer Bundesausschuss

Durvalumab

Resolution from: 1 April 2021 valid until: unlimited
Entry into force on: 1 April 2021
BAnz AT 04.05.2021 B6

New therapeutic indication (according to the marketing authorisation of 27 August 2020):

Imfinzi in combination with etoposide and either carboplatin or cisplatin is indicated for the first-line treatment of adults with extensive-stage small cell lung cancer (ES-SCLC).

Therapeutic indication of the resolution (resolution from 1 April 2021):

see new therapeutic indication according to marketing authorisation

1. Additional benefit of the medicinal product in relation to the appropriate comparator therapy

Adult patients with extensive-stage small cell lung cancer (ES-SCLC); for first-line treatment

Appropriate comparator therapy:

- Cisplatin in combination with etoposide

or

- Carboplatin in combination with etoposide

or

- Atezolizumab in combination with carboplatin and etoposide

Extent and probability of the additional benefit of durvalumab compared to cisplatin in combination with etoposide or carboplatin in combination with etoposide:

Hint for a minor additional benefit

Study results according to endpoints:[1]

CASPIAN study: Durvalumab + chemotherapy[2] vs durvalumab + tremelimumab + chemotherapy[2] vs chemotherapy[2] (global cohort and cohort in China)

Study design: RCT, open, phase III

Relevant study arms: Durvalumab + chemotherapy[2] vs chemotherapy[2]

Data cut-offs:

- Global cohort: 27 January 2020 (final analysis of overall survival)
- Cohort in China: 6 January 2020 (analysis of overall survival)

Summary of results for relevant clinical endpoints

Endpoint category	Direction of effect/ Risk of bias	Summary
Mortality	↑	Advantage in overall survival
Morbidity	↔	no relevant difference for the benefit assessment
Health-related quality of life	↔	no relevant difference for the benefit assessment
Side effects	↔	no relevant difference for the benefit assessment
Explanations: ↑: statistically significant and relevant positive effect with low/unclear reliability of data ↓: statistically significant and relevant negative effect with low/unclear reliability of data ↑↑: statistically significant and relevant positive effect with high reliability of data ↓↓: statistically significant and relevant negative effect with high reliability of data ↔: no statistically significant or relevant difference ∅: There is no usable data for the benefit assessment. n.a.: not assessable		

[1] Data from the dossier evaluation of the IQWiG (A20-87) and from the addendum (A21-19), unless otherwise indicated.

[2] Chemotherapy: Cisplatin + etoposide *or* carboplatin + etoposide

Mortality

Endpoint	Durvalumab + chemotherapy[a]		Chemotherapy[a]		Intervention vs control
	N	Median time to event in months [95% CI] *Patients with event n (%)*	N	Median time to event in months [95% CI] *Patients with event n (%)*	Hazard ratio [95% CI] p value Absolute difference (AD)[b]
Overall survival					
Global cohort	268	12.9 [11.3; 14.7] *210 (78.4)*	269	10.5 [9.3; 11.2] *231 (85.9)*	0.75 [0.63; 0.91] 0.003 AD: +2.4 months
Cohort in China	61	14.4 [12.3; n. a.] *35 (57.4)*	62	10.9 [8.9; 14.0] *43 (69.4)*	0.65 [0.41; 1.03] 0.066
Total[c, d]	328	13.4 [11.9; 14.7] *245 (74.7)*	330	10.6 [9.5; 11.2] *273 (82.7)*	0.74 [0.63; 0.88] < 0.001 AD: +2.8 months

Morbidity

Endpoint	Durvalumab + chemotherapy[a]		Chemotherapy[a]		Intervention vs control
	N	Median time to event in months [95% CI] *Patients with event n (%)*	N	Median time to event in months [95% CI] *Patients with event n (%)*	Hazard ratio [95% CI] p value Absolute difference (AD)[b]
Progression-free survival (PFS)[3]					
Global cohort	268	5.1 [4.7; 6.2] *234 (87.3)*	269	5.4 [4.8; 6.2] *236 (87.7)*	0.80 [0.67; 0.96] 0.016 AD: -0.3 months
Cohort in China	61	4.9 [4.7; 5.5] *54 (88.5)*	62	5.5 [4.9; 6.3] *50 (80.6)*	1.00 [0.68; 1.48] 0.998
Total[c,d]	328	5.0 [4.7; 5.6] *287 (87.5)*	330	5.4 [4.9; 6.1] *285 (86.4)*	0.83 [0.70; 0.98] 0.027 AD: -0.4 months

[3] Data from the dossier Durvalumab Modul 4A of 23.09.2020

Morbidity

Endpoint	Durvalumab + chemotherapy[a]			Chemotherapy[a]			Intervention vs control
	N[e]	Values at the start of the study MV (SD)	Mean change in the course of study up to 12 months MV (SE)	N[e]	Values at the start of the study MV (SD)	Mean change in the course of study up to 12 months MV (SE)	Mean difference [95% CI] p value
EORTC QLQ-C30 (symptom scales)[f]							
Fatigue							
Global cohort[g]	233	35.32 (24.59)	−7.47 (1.63)	233	37.14 (27.21)	-5.21 (1.84)	-2.27 [-5.52; 0.98] 0.171
Cohort in China	58	26.05 (18.45)	-0.36 (2.12)	56	22.03 (17.60)	n.a.	n.a.
Total[d,h]	290	33.66 (23.76)	-6.78 (1.33)	288	34.25 (26.35)	-5.56 (1.51)	-1.22 [-4.08; 1.64] 0.402
Nausea and vomiting							
Global cohort[g]	233	5.56 (13.75)	-0.65 (0.92)	233	6.94 (16.79)	1.54 (1.07)	-2.20 [-4.04; -0.35] 0.020
Cohort in China	58	3.45 (10.71)	n.a.	56	2.87 (8.34)	n.a.	n.a.
Total[d,h]	290	5.17 (13.25)	0.62 (0.80)	288	6.13 (15.62)	2.40 (0.92)	-1.78 [-3.48; -0.08] 0.040 Hedges´ g[i]: -0.17 [-0.34; -0.01]
Pain							
Global cohort[g]	233	28.25 (26.73)	-11.75 (1.56)	233	29.52 (29.52)	-12.12 (1.81)	0.37 [-2.92; 3.65] 0.827
Cohort in China	58	20.11 (22.89)	n.a.	56	21.26 (20.89)	n.a.	n.a.
Total[d,h]	290	26.73 (26.24)	-10.06 (1.27)	288	27.87 (28.25)	-10.81 (1.47)	0.75 [-2.10; 3.60] 0.606

Endpoint	Durvalumab + chemotherapy[a]			Chemotherapy[a]			Intervention vs control
	N[e]	Values at the start of the study MV (SD)	Mean change in the course of study up to 12 months MV (SE)	N[e]	Values at the start of the study MV (SD)	Mean change in the course of study up to 12 months MV (SE)	Mean difference [95% CI] p value
Dyspnoea							
Global cohort[g]	233	36.31 (28.73)	-12.69 (1.86)	233	38.50 (30.64)	-12.96 (2.16)	0.27 [-3.64; 4.19] 0.891
Cohort in China	58	28.16 (24.02)	-9.82 (2.16)	56	25.86 (25.01)	n.a.	n.a.
Total[d,h]	290	34.87 (28.02)	-12.39 (1.54)	288	36.09 (30.07)	-11.81 (1.78)	-0.58 [-3.98; 2.82] 0.737
Insomnia							
Global cohort[g]	233	29.81 (31.68)	-13.51 (1.86)	233	33.88 (35.58)	-12.16 (2.13)	-1.35 [-5.10; 2.40] 0.480
Cohort in China	58	17.24 (20.94)	n.a.	56	17.24 (19.98)	n.a.	n.a.
Total[d,h]	290	27.50 (30.31)	-10.96 (1.50)	288	30.68 (33.83)	-9.79 (1.71)	-1.17 [-4.39; 2.05] 0.476
Loss of appetite							
Global cohort[g]	233	24.12 (30.21)	-12.75 (1.66)	233	25.58 (32.49)	-7.42 (1.92)	-5.33 [-8.66; -2.00] 0.002
Cohort in China	58	14.94 (24.32)	n.a.	56	20.11 (23.31)	n.a.	n.a.
Total[d,h]	290	22.44 (29.38)	-9.90 (1.36)	288	24.50 (31.03)	-5.74 (1.57)	-4.16 [-7.06; -1.27] 0.005 Hedges´ g[i]: -0.24 [-0.40; -0.07]

Endpoint	Durvalumab + chemotherapy[a]			Chemotherapy[a]			Intervention vs control
	N[e]	Values at the start of the study MV (SD)	Mean change in the course of study up to 12 months MV (SE)	N[e]	Values at the start of the study MV (SD)	Mean change in the course of study up to 12 months MV (SE)	Mean difference [95% CI] p value
Constipation							
Global cohort[g]	233	12.20 (23.04)	-2.24 (1.57)	233	18.10 (29.48)	-3.87 (1.87)	1.63 [-1.84; 5.10] 0.356
Cohort in China	58	10.92 (20.12)	-3.14 (1.99)	56	13.22 (18.67)	n.a.	n.a.
Total[d,h]	290	11.99 (22.52)	-2.23 (1.28)	288	17.00 (27.67)	-4.06 (1.54)	1.83 [-1.19; 4.84] 0.235
Diarrhoea							
Global cohort[g]	233	4.88 (14.87)	-2.82 (0.74)	233	5.58 (15.99)	-1.22 (0.90)	-1.60 [-3.13; -0.07] 0.041
China	58	1.15 (6.14)	n.a.	56	2.30 (8.52)	n.a.	n.a.
Total[d,h]	290	4.18 (13.73)	-2.86 (0.57)	288	4.97 (14.92)	-1.49 (0.72)	-1.37 [-2.69; -0.05] 0.043 Hedges´ g[i] -0.17 [-0.33; -0.01]
EORTC QLQ-LC13 (symptom scales)[d]							
Alopecia							
Global cohort[g]	232	1.90 (10.28)	15.83 (1.49)	232	2.99 (12.08)	21.68 (1.90)	-5.85 [-10.03; -1.68] 0.006
Cohort in China	58	6.32 (13.18)	n.a.	56	6.32 (13.18)	n.a.	n.a.
Total[d,h]	289	2.76 (11.03)	17.03 (1.25)	287	3.64 (12.36)	22.90 (1.60)	-5.88 [-9.48; -2.28] 0.001 Hedges' g[i]: -0.27 [-0.43; -0.10]

Endpoint	Durvalumab + chemotherapy[a]			Chemotherapy[a]			Intervention vs control
	N[e]	Values at the start of the study MV (SD)	Mean change in the course of study up to 12 months MV (SE)	N[e]	Values at the start of the study MV (SD)	Mean change in the course of study up to 12 months MV (SE)	Mean difference [95% CI] p value
Hemoptysis							
Global cohort[g]	232	6.26 (16.44)	-4.69 (0.52)	232	5.31 (14.28)	-4.68 (0.67)	-0.02 [-1.25; 1.22] 0.981
Cohort in China	58	9.20 (17.43)	−7.69 (1.05)	56	8.62 (15.99)	n.a.	n.a.
Total[d,h]	289	6.84 (16.67)	-4.99 (0.43)	287	5.96 (14.68)	-4.64 (0.58)	-0.35 [-1.47; 0.78] 0.544
Dysphagia							
Global cohort[g]	232	9.52 (20.69)	-4.72 (0.99)	232	9.39 (22.13)	-3.82 (1.21)	-0.90 [-3.16; 1.35] 0.431
Cohort in China	58	9.20 (17.43)	n.a.	56	7.47 (18.78)	n.a.	n.a.
Total[d,h]	289	9.49 (20.12)	-4.25 (0.82)	287	9.05 (21.54)	-3.53 (1.01)	-0.73 [-2.70; 1.25] 0.469
Dyspnoea							
Global cohort[g]	232	30.70 (23.49)	-8.66 (1.44)	232	31.75 (23.91)	-7.55 (1.62)	-1.12 [-3.97; 1.73] 0.441
Cohort in China	58	27.78 (21.15)	-5.22 (1.56)	56	23.56 (20.51)	n.a.	n.a.
Total[d,h]	289	30.21 (23.07)	-7.63 (1.18)	287	30.13 (23.51)	-6.98 (1.32)	-0.65 [-3.13; 1.82] 0.604
Cough							
Global cohort[g]	232	41.50 (25.90)	-17.20 (1.68)	232	40.54 (26.44)	-16.95 (2.01)	-0.25 [-3.98; 3.48] 0.895
Cohort in China	58	39.08 (24.29)	-20.15 (2.67)	56	36.21 (26.70)	n.a.	n.a.
Total[d,h]	289	40.95 (25.58)	-18.08 (1.41)	287	39.74 (26.54)	-17.18 (1.71)	-0.90 [-4.24; 2.44] 0.596

Endpoint	Durvalumab + chemotherapy[a]			Chemotherapy[a]			Intervention vs control
	N[e]	Values at the start of the study MV (SD)	Mean change in the course of study up to 12 months MV (SE)	N[e]	Values at the start of the study MV (SD)	Mean change in the course of study up to 12 months MV (SE)	Mean difference [95% CI] p value
Mouth pain							
Global cohort[g]	232	4.76 (14.78)	-0.84 (0.95)	232	-0.37 (1.15)	4.22 (13.34)	-0.47 [-2.53; 1.59] 0.655
Cohort in China	58	4.02 (10.95)	n.a.	56	3.45 (10.24)	n.a.	n.a.
Total[d,h]	289	4.64 (14.12)	-0.25 (0.76)	287	4.08 (12.81)	0.04 (0.94)	-0.29 [-2.08; 1.49] 0.749
Peripheral neuropathy							
Global cohort[g]	232	9.12 (21.41)	4.09 (1.65)	232	8.57 (19.42)	7.50 (2.03)	-3.41 [-7.38; 0.56] 0.092
Cohort in China	58	7.47 (18.78)	-0.14 (1.70)	56	4.02 (12.61)	n.a.	n.a.
Total[d,h]	289	8.83 (20.94)	2.41 (1.34)	287	7.73 (18.41)	5.11 (1.65)	-2.71 [-6.09; 0.68] 0.117
Pain (arm/shoulder)							
Global cohort[g]	232	16.87 (24.82)	-4.00 (1.45)	232	13.20 (24.76)	-4.69 (1.75)	0.69 [-2.62; 3.99] 0.683
Cohort in China	58	18.97 (26.57)	n.a.	56	7.47 (14.02)	n.a.	n.a.
Total[d,h]	289	17.22 (25.16)	-3.61 (1.20)	287	12.03 (23.19)	-4.43 (1.47)	0.82 [-2.09; 3.73] 0.580
Pain (chest)							
Global cohort[g]	232	22.72 (25.53)	-8.58 (1.58)	232	21.09 (25.15)	-8.38 (1.82)	-0.2 [-3.50; 3.10] 0.906
Cohort in China	58	24.71 (30.31)	-6.74 (2.23)	56	20.11 (23.31)	n.a.	n.a.
Total[d,h]	289	23.18 (26.48)	-8.70 (1.28)	287	20.86 (24.81)	-8.66 (1.48)	-0.04 [-2.91; 2.83] 0.980

Endpoint	Durvalumab + chemotherapy[a]			Chemotherapy[a]			Intervention vs control
	N[e]	Values at the start of the study MV (SD)	Mean change in the course of study up to 12 months MV (SE)	N[e]	Values at the start of the study MV (SD)	Mean change in the course of study up to 12 months MV (SE)	Mean difference [95% CI] p value
Pain (other)							
Global cohort[g]	232	21.36 (27.53)	-5.52 (1.70)	232	22.99 (30.06)	-4.79 (2.01)	-0.73 [-4.48; 3.03] 0.703
Cohort in China	58	17.24 (22.72)	-4.34 (1.99)	56	19.54 (25.77)	n.a.	n.a.
Total[d,h]	289	20.64 (26.71)	-5.57 (1.37)	287	22.30 (29.32)	-5.18 (1.63)	-0.39 [-3.59; 2.81] 0.811
Health status (EQ-5D VAS)							
Global cohort[g]	228	63.7 (19.91)	7.76 (1.28)	228	61.0 (20.43)	6.83 (1.44)	0.93 [-1.63; 3.49] 0.477
Cohort in China	58	72.1 (17.93)	2.00 (1.58)	56	68.9 (22.04)	n.a.	n.a.
Total[d,h]	285	65.2 (19.80)	7.02 (1.06)	283	62.5 (20.97)	6.48 (1.17)	0.54 [-1.68; 2.76] 0.631
Patient's Global Impression of Change (PGIC)							
no usable data available							

Health-related quality of life[j]

Endpoint	Durvalumab + chemotherapy[a]			Chemotherapy[a]			Intervention vs control
	N[e]	Values at the start of the study MV (SD)	Mean change in the course of study up to 12 months MV (SE)	N[e]	Values at the start of the study MV (SD)	Mean change in the course of study up to 12 months MV (SE)	Mean difference [95% CI] p value
EORTC QLQ-C30 (functional scales)							
Global health status							
Global cohort[g]	233	56.06 (22.21)	11.23 (1.45)	233	54.08 (22.41)	9.30 (1.63)	1.93 [-0.92; 4.78] 0.184
Cohort in China	58	60.78 (20.35)	6.15 (1.62)	56	61.21 (23.55)	n.a.	n.a.
Total[d,h]	290	56.88 (21.90)	10.42 (1.19)	288	55.52 (22.77)	9.17 (1.33)	1.24 [-1.25; 3.73] 0.327
Physical functioning							
Global cohort[g]	233	72.22 (21.25)	7.01 (1.49)	233	70.67 (22.42)	5.95 (1.65)	1.07 [-1.83; 3.97] 0.470
Cohort in China	58	81.95 (16.89)	-0.65 (1.49)	56	82.18 (16.68)	n.a.	n.a.
Total[d,h]	290	74.02 (20.82)	5.70 (1.21)	288	72.87 (21.93)	5.40 (1.33)	0.30 [-2.21; 2.81] 0.815
Role function							
Global cohort[g]	233	69.99 (29.99)	7.44 (1.88)	233	69.80 (31.13)	3.73 (2.09)	3.71 [0.10; 7.32] 0.044
Cohort in China	58	79.02 (25.47)	-0.74 (2.31)	56	81.03 (25.26)	n.a.	n.a.
Total[d,h]	290	71.73 (29.41)	6.88 (1.56)	288	71.96 (30.43)	4.52 (1.72)	2.36 [-0.84; 5.56] 0.148

Endpoint	Durvalumab + chemotherapy[a]			Chemotherapy[a]			Intervention vs control
	N[e]	Values at the start of the study MV (SD)	Mean change in the course of study up to 12 months MV (SE)	N[e]	Values at the start of the study MV (SD)	Mean change in the course of study up to 12 months MV (SE)	Mean difference [95% CI] p value
Emotional function							
Global cohort[g]	233	73.71 (21.39)	10.04 (1.40)	233	71.73 (24.96)	8.79 (1.60)	1.25 [-1.66; 4.16] 0.399
Cohort in China	58	84.63 (16.94)	1.31 (1.58)	56	85.34 (15.48)	n.a.	n.a.
Total[d,h]	290	75.83 (21.06)	8.23 (1.18)	288	74.28 (24.04)	7.98 (1.33)	0.24 [-2.32; 2.81] 0.852
Cognitive function							
Global cohort[g]	233	87.06 (19.48)	2.34 (1.21)	233	86.94 (19.43)	-0.77 (1.39)	3.11 [0.61; 5.61] 0.015
Cohort in China	58	90.23 (13.62)	-5.47 (1.65)	56	91.09 (13.69)	n.a.	n.a.
Total[d,h]	290	87.68 (18.56)	0.75 (1.03)	288	87.80 (18.51)	-1.02 (1.16)	1.77 [-0.44; 3.99] 0.117
Social function							
Global cohort[g]	233	76.90 (27.44)	7.12 (1.70)	233	76.26 (27.49)	5.34 (1.90)	1.78 [-1.60; 5.16] 0.302
Cohort in China	58	73.85 (24.80)	0.37 (2.67)	56	77.30 (24.92)	n.a.	n.a.
Total[d,h]	290	76.35 (26.99)	4.29 (1.42)	288	76.55 (26.98)	3.21 (1.58)	1.08 [-1.92; 4.08] 0.478

Side effects

Endpoint	Durvalumab + chemotherapy[a]		Chemotherapy[a]		Intervention vs control
	N	Median time to event in months [95% CI] *Patients with event n (%)*	N	Median time to event in months [95% CI] *Patients with event n (%)*	Hazard ratio [95% CI] p value Absolute difference (AD)[b]
Adverse events (presented additionally)					
Global cohort	265	0.3 [0.2; 0.3] *260 (98.1)*	266	0.3 [0.2; 0.3] *258 (97.0)*	–
Cohort in China	61	0.1 [0.1; 0.1] *61 (100.0)*	62	0.1 [0.1; 0.1] *61 (98.4)*	–
Total[c,d]	325	0.3 [0.2; 0.3] *320 (98.5)*	327	0.2 [0.2; 0.3] *318 (97.2)*	–
Serious adverse events (SAE)					
Global cohort	265	n. a. [21.6; n. c.] *85 (32.1)*	266	n.a. *97 (36.5)*	0.72 [0.53; 0.97] 0.030 AD: n.a.
Cohort in China	61	n. a. [3.9; n. c.] *26 (42.6)*	62	n.a. *22 (35.5)*	1.11 [0.63; 1.99] 0.714
Total[c,d]	325	n. a. [21.6; n. c.] *110 (33.8)*	327	n.a. *119 (36.4)*	0.78 [0.60; 1.02] 0.067
Effect modification by the feature “brain metastases at the start of the study“					
Presence of brain metastases at the start of the study					
	37	n. a. [12.4; n. c.] *9 (24.3)*	37	3.0 [1.5; n. a.] *19 (51.4)*	0.35 [0.14; 0.77] 0.009 AD: n.a.
No presence of brain metastases at the start of the study					
	288	n. a. [21.6; n. c.] *101 (35.1)*	299	n.a. *100 (34.5)*	0.87 [0.65; 1.15] 0.320
Total				Interaction:	0.030

Endpoint	Durvalumab + chemotherapy[a]		Chemotherapy[a]		Intervention vs control
	N	Median time to event in months [95% CI] *Patients with event n (%)*	N	Median time to event in months [95% CI] *Patients with event n (%)*	Hazard ratio [95% CI] p value Absolute difference (AD)[b]
Severe adverse events (CTCAE grade> 3)[k]					
Global cohort	265	0.7 [0.5; 1.0] *171 (64.5)*	266	0.7 [0.5; 0.8] *173 (65.0)*	0.98 [0.80; 1.21] 0.873
Cohort in China	61	0.1 [0.1; 0.2] *49 (80.3)*	62	0.1 [0.1; 0.2] *49 (79.0)*	0.99 [0.66; 1.47] 0.954
Total[c,d]	325	0.5 [0.3; 0.7] *219 (67.4)*	327	0.5 [0.3; 0.7] *222 (67.9)*	0.98 [0.81; 1.18] 0.801
Discontinuation because of adverse events[l]					
Global cohort	265	n.a. *27 (10.2)*	266	n.a. *25 (9.4)*	0.90 [0.51; 1.59] 0.718
Cohort in China	61	n.a. *10 (16.4)*	62	n.a. *7 (11.3)*	1.27 [0.47; 3.54] 0.639
Total[c,d]	325	n.a. *37 (11.4)*	327	n.a. *32 (9.8)*	0.98 [0.60; 1.60] 0.938
Immune-mediated adverse events (presented additionally)					
Global cohort	265	21.6 [11.2; n. a.] *95 (35.8)*	266	n.a. *60 (22.6)*	–
Cohort in China	61	6.2 [4.9; n. a.] *28 (45.9)*	62	n.a. *11 (17.7)*	–
Total[c,d]	325	14.5 [10.4; n. a.] *123 (37.8)*	327	n.a. *71 (21.7)*	–
Immune-mediated serious adverse events (SAE)					
Global cohort	265	n.a. *9 (3.4)*	266	n.a. *8 (3.0)*	0.70 [0.24; 1.99] 0.504
Cohort in China	61	n.a. *3 (4.9)*	62	n.a. *0 (0)*	n. d.[m]
Total[c,d]					Heterogeneity: p = 0.0497

Endpoint	Durvalumab + chemotherapy[a]		Chemotherapy[a]		Intervention vs control
	N	Median time to event in months [95% CI] *Patients with event n (%)*	N	Median time to event in months [95% CI] *Patients with event n (%)*	Hazard ratio [95% CI] p value Absolute difference (AD)[b]
Immune-mediated serious adverse events [k]					
Global cohort	265	n.a. *12 (4.5)*	266	n.a. *6 (2.3)*	1.54 [0.57; 4.56] 0.340
Cohort in China	61	n.a. *2 (3.3)*	62	n.a. *0 (0)*	n. d.[m]
Total[c,d]	325	n.a. *14 (4.3)*	327	n.a. *6 (1.8)*	1.87 [0.72; 5.41] 0.120
Effect modification by the feature “Gender“					
Male					
	240	n.a. *8 (3.3)*	232	n.a. *6 (2.6)*	1.15 [0.39; 3.52] 0.797
Female					
	85	n.a. *6 (7.1)*	95	n.a. *0 (0)*	n. c. no data[m]
				Interaction:	0.018
PRO-CTCAE					
Global cohort	no usable data available				
Cohort in China	Endpoint not surveyed				
Hypertonia (PT, severe AEs)					
Global cohort	265	n.a. *8 (3.0)*	266	n.a. *1 (0.4)*	7.77 [1.42; 144.07] 0.014 AD: n.a.
Cohort in China	61	n.a. *3 (4.9)*	62	n.a. *1 (1.6)*	3.13 [0.40; 63.22] 0.287
Total[c,d]	325	n.a. *11 (3.4)*	327	n.a. *2 (0.6)*	5.46 [1.47; 35.28] 0.009 AD: n.a.

Endpoint	Durvalumab + chemotherapy[a]		Chemotherapy[a]		Intervention vs control
	N	Median time to event in months [95% CI] *Patients with event n (%)*	N	Median time to event in months [95% CI] *Patients with event n (%)*	Hazard ratio [95% CI] p value Absolute difference (AD)[b]
Blood and lymphatic system disorders (SOC, severe adverse events[k])					
Global cohort	265	n.a. *95 (35.8)*	266	n. a. [2.5; n. c.] *125 (47.0)*	0.71 [0.54; 0.92] 0.010 AD: n.a.
Cohort in China	61	n. a. [1.4; n. c.] *29 (47.5)*	62	2.3 [0.7; n. a.] *34 (54.8)*	0.78 [0.47; 1.28] 0.332
Total[c,d]	325	n.a. *124 (38.2)*	327	4.0 [2.3; n. a.] *159 (48.6)*	0.72 [0.57; 0.91] 0.006 AD: n.a.
Effect modification by the feature “brain metastases at the start of the study“					
Presence of brain metastases at the start of the study					
	37	n.a. *10 (27.0)*	37	0.7 [0.5; 2.1] *28 (75.7)*	0.24 [0.11; 0.49] 0.001 AD: n.a.
No presence of brain metastases at the start of the study					
	288	n.a. *114 (39.6)*	290	n. a. [3.2; n. c.] *131 (45.2)*	0.84 [0.65; 1.07] 0.161
Total				Interaction:	< 0.001

Endpoint	Durvalumab + chemotherapy[a]		Chemotherapy[a]		Intervention vs control
	N	Median time to event in months [95% CI] *Patients with event n (%)*	N	Median time to event in months [95% CI] *Patients with event n (%)*	Hazard ratio [95% CI] p value Absolute difference (AD)[b]

[a] Cisplatin in combination with etoposide or carboplatin in combination with etoposide
[b] Information only in case of significant difference
[c] calculated by meta-analysis
[d] A total of 2 patients were included in both the China cohort and the global cohort. These patients were assigned to the cohort in China for the meta-analysis.
[e] Number of patients who were taken into account in the evaluation for calculating the effect estimate; the values at the start of the study (possibly at other times) can be based on other patient numbers.
[f] Lower (decreasing) values mean better symptomatology; negative effects (intervention minus control) mean an advantage for the intervention.
[g] Patients from 1 study centre in Ukraine were not included due to incorrect data collection. These included 16 (information in the study report) or 17 (information in the SAP) randomised patients.
[h] for the meta-analysis additionally adjusted for cohort (global vs China)
[i] IQWiG calculations
[j] Higher (increasing) values mean better quality of life; positive effects (intervention minus control) mean an advantage for the intervention.
[k] operationalised as CTCAE grade ≥ 3
[l] Discontinuation of at least one active ingredient component
[m] p value cannot be calculated based on likelihood ratio test

CTCAE: Common Terminology Criteria for Adverse Events; EORTC: European Organization for Research and Treatment of Cancer; EQ-5D: Quality of Life Questionnaire 5 Dimensions; HR: hazard ratio; n. d.: no data; CI: confidential interval; MMRM: mixed model for repeated measures; MD: mean difference; MV: mean value; N: number of patients evaluated; n: Number of patients with (at least 1) event; n. c.: not calculable; n.a.:not achieved; PRO: Patient-Reported Outcome; PT: preferred term; QLQ-C30: Quality of Life Questionnaire–Cancer 30; QLQ-LC-13: Quality of Life Questionnaire–Lung Cancer 13; RCT: randomised controlled trial; SAP: statistical analysis plan; SD: standard deviation; SE: standard error; SOC: system organ class; VAS: visual analogue scale

2. Number of patients or demarcation of patient groups eligible for treatment

Adult patients with extensive-stage small cell lung cancer (ES-SCLC); first-line treatment

approx. 3210 – 6130 patients

3. Requirements for a quality-assured application

The requirements in the product information are to be taken into account. The European Medicines Agency (EMA) provides the contents of the product information (summary of product characteristics, SmPC) for Imfinzi (active ingredient: durvalumab) at the following publicly accessible link (last access: 4. February 2021):

https://www.ema.europa.eu/documents/product-information/imfinzi-epar-product-information_de.pdf

Treatment with durvalumab may only be initiated and monitored by specialists in internal medicine, haematology and oncology who are experienced in the treatment of patients with small-cell lung cancer, as well as specialists in internal medicine and pulmonology or specialists in pulmonary medicine and doctors from other specialist groups participating in the Oncology Agreement.

Patients with symptomatic brain metastases were excluded from the CASPIAN study. No data are available for patients with symptomatic brain metastases.

4. Treatment costs

Annual treatment costs:

The annual treatment costs shown refer to the first year of treatment.

Adult patients with extensive-stage small-cell lung cancer (ES-SCLC); for first-line treatment

Designation of the therapy	Annual treatment costs/patient
Medicinal product to be assessed:	
Induction therapy with cisplatin	
Durvalumab	€ 27,972.48
Cisplatin	€ 455.80 – € 520.64
Etoposide	€ 918.00
Total	€ 29,346.28 – € 29,411.12
additionally required SHI services	€ 123.48 – € 158.09
Induction therapy with carboplatin	
Durvalumab	€ 27,972.48
Carboplatin	€ 1,576.72 – 1,887.20
Etoposide	€ 918.00
Total	€ 30,467.20 – € 30,777.68
Maintenance treatment	
Durvalumab	€ 69,931.20
Appropriate comparator therapy:	
Cisplatin + etoposide	
Cisplatin	€ 1,982.73
Etoposide	€ 3,993.30
Total	€ 5,976.03
additionally required SHI services	€ 328.58 – € 421.62
Carboplatin + etoposide	
Carboplatin	€ 6,858.73

Designation of the therapy	Annual treatment costs/patient
Etoposide	€ 3,993.30
Total	€ 10,852.03
Atezolizumab + carboplatin + etoposide	
Induction therapy	
Atezolizumab	€ 15,578.60
Carboplatin	€ 1,576.72
Etoposide	€ 918.00
Total	€ 18,073.32
Maintenance treatment	
Atezolizumab	€ 52,188.31

Costs after deduction of statutory rebates (LAUER-TAXE®, as last revised: 15 March 2021)

Other SHI services:

Designation of the therapy	Type of service	Costs/ unit	Number/ cycle	Number/ patient/ year	Costs/ patient/ year
Medicinal product to be assessed:					
Durvalumab	Surcharge for the preparation of a parenteral solution containing monoclonal antibodies	€ 71	1	14	€ 994
Cisplatin	Surcharge for production of a parenteral preparation containing cytostatic agents	€ 81	1	4	€ 324
Carboplatin	Surcharge for production of a parenteral preparation containing cytostatic agents	€ 81	1	4	€ 324
Etoposide	Surcharge for production of a parenteral preparation containing cytostatic agents	€ 81	3	12	€ 972
Appropriate comparator therapy:					

Designation of the therapy	Type of service	Costs/ unit	Number/ cycle	Number/ patient/ year	Costs/ patient/ year
Cisplatin	Surcharge for production of a parenteral preparation containing cytostatic agents	€ 81	1	17.4	€ 1,409.40
Carboplatin	Surcharge for production of a parenteral preparation containing cytostatic agents	€ 81	1	17.4	€ 1,409.40
Etoposide	Surcharge for production of a parenteral preparation containing cytostatic agents	€ 81	3	52.2	€ 4,228.20
Atezolizumab + carboplatin + etoposide					
Atezolizumab	Surcharge for the preparation of a parenteral solution containing monoclonal antibodies	€ 71	1	17.4	€ 1,235.40
Carboplatin	Surcharge for production of a parenteral preparation containing cytostatic agents	€ 81	1	4	€ 324
Etoposide	Surcharge for production of a parenteral preparation containing cytostatic agents	€ 81	3	12	€ 972