# Resolution

Gemeinsamer Bundesausschuss

## of the Federal Joint Committee on an amendment to the Pharmaceuticals Directive Annex XII – Benefit Assessment of Medicinal Products with New Active Ingredients according to Section 35a SGB V Durvalumab (New Therapeutic Indication: Small Cell Lung Cancer, First-line, in Combination with Etoposid and either Carboplatin or Cisplatin)

From 1. April 2021
At its session on 1. April 2021, the Federal Joint Committee (G-BA) resolved to amend the Directive on the Prescription of Medicinal Products in SHI-accredited Medical Care (Pharmaceuticals Directive, AM-RL) in the version dated 18 December 2008/22 January 2009 (Federal Gazette, BAnz. No. 49a of 31 March 2009), as last amended on DD Month YYYY (Federal Gazette, BAnz AT DD MM YYYY BX), as follows:

**I. In Annex XII, the following information shall be added after No. 4 to the information on the benefit assessment of durvalumab in accordance with the resolution of 4 April 2019:**

**Durvalumab**

Resolution from: 1 April 2021
Entry into force on: 1 April 2021
BAnz AT DD MM YYYY Bx

**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:<br>↑: statistically significant and relevant positive effect with low/unclear reliability of data<br>↓: statistically significant and relevant negative effect with low/unclear reliability of data<br>↑↑: statistically significant and relevant positive effect with high reliability of data<br>↓↓: statistically significant and relevant negative effect with high reliability of data<br>↔: no statistically significant or relevant difference<br>∅: There is no usable data for the benefit assessment.<br>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]<br>*Patients with event n (%)* | N | Median time to event in months [95% CI]<br>*Patients with event n (%)* | Hazard ratio [95% CI]<br>p value<br>Absolute difference (AD)[b] |
| **Overall survival** | | | | | |
| Global cohort | 268 | 12.9 [11.3; 14.7]<br>*210 (78.4)* | 269 | 10.5 [9.3; 11.2]<br>*231 (85.9)* | 0.75<br>[0.63; 0.91]<br>0.003<br>AD: +2.4 months |
| Cohort in China | 61 | 14.4 [12.3; n. a.]<br>*35 (57.4)* | 62 | 10.9 [8.9; 14.0]<br>*43 (69.4)* | 0.65<br>[0.41; 1.03]<br>0.066 |
| Total[c, d] | 328 | 13.4 [11.9; 14.7]<br>*245 (74.7)* | 330 | 10.6 [9.5; 11.2]<br>*273 (82.7)* | 0.74<br>[0.63; 0.88]<br>< 0.001<br>AD: +2.8 months |

**Morbidity**

| Endpoint | Durvalumab + chemotherapy[a] | | Chemotherapy[a] | | Intervention vs control |
|---|---|---|---|---|---|
| | N | Median time to event in months [95% CI]<br>*Patients with event n (%)* | N | Median time to event in months [95% CI]<br>*Patients with event n (%)* | Hazard ratio [95% CI]<br>p value<br>Absolute difference (AD)[b] |
| **Progression-free survival (PFS)[3]** | | | | | |
| Global cohort | 268 | 5.1 [4.7; 6.2]<br>*234 (87.3)* | 269 | 5.4 [4.8; 6.2]<br>*236 (87.7)* | 0.80<br>[0.67; 0.96]<br>0.016<br>AD: -0.3 months |
| Cohort in China | 61 | 4.9 [4.7; 5.5]<br>*54 (88.5)* | 62 | 5.5 [4.9; 6.3]<br>*50 (80.6)* | 1.00<br>[0.68; 1.48]<br>0.998 |
| Total[c,d] | 328 | 5.0 [4.7; 5.6]<br>*287 (87.5)* | 330 | 5.4 [4.9; 6.1]<br>*285 (86.4)* | 0.83<br>[0.70; 0.98]<br>0.027<br>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<br>MV (SD) | Mean change in the course of study up to 12 months<br>MV (SE) | N[e] | Values at the start of the study<br>MV (SD) | Mean change in the course of study up to 12 months<br>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<br>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<br>MV (SD) | Mean change in the course of study up to 12 months<br>MV (SE) | N[e] | Values at the start of the study<br>MV (SD) | Mean change in the course of study up to 12 months<br>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<br>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<br>MV (SD) | Mean change in the course of study up to 12 months<br>MV (SE) | N[e] | Values at the start of the study<br>MV (SD) | Mean change in the course of study up to 12 months<br>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<br>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<br>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<br>MV (SD) | Mean change in the course of study up to 12 months<br>MV (SE) | N[e] | Values at the start of the study<br>MV (SD) | Mean change in the course of study up to 12 months<br>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<br>MV (SD) | Mean change in the course of study up to 12 months<br>MV (SE) | N[e] | Values at the start of the study<br>MV (SD) | Mean change in the course of study up to 12 months<br>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<br>MV (SD) | Mean change in the course of study up to 12 months<br>MV (SE) | N[e] | Values at the start of the study<br>MV (SD) | Mean change in the course of study up to 12 months<br>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<br>MV (SD) | Mean change in the course of study up to 12 months<br>MV (SE) | N[e] | Values at the start of the study<br>MV (SD) | Mean change in the course of study up to 12 months<br>MV (SE) | Mean difference [95% CI]<br>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]<br>*Patients with event n (%)* | N | Median time to event in months [95% CI]<br>*Patients with event n (%)* | Hazard ratio [95% CI]<br>p value<br>Absolute difference (AD)[b] |
| **Adverse events (presented additionally)** | | | | | |
| Global cohort | 265 | 0.3 [0.2; 0.3]<br>*260 (98.1)* | 266 | 0.3 [0.2; 0.3]<br>*258 (97.0)* | – |
| Cohort in China | 61 | 0.1 [0.1; 0.1]<br>*61 (100.0)* | 62 | 0.1 [0.1; 0.1]<br>*61 (98.4)* | – |
| Total[c,d] | 325 | 0.3 [0.2; 0.3]<br>*320 (98.5)* | 327 | 0.2 [0.2; 0.3]<br>*318 (97.2)* | – |
| **Serious adverse events (SAE)** | | | | | |
| Global cohort | 265 | n. a. [21.6; n. c.]<br>*85 (32.1)* | 266 | n.a.<br>*97 (36.5)* | 0.72<br>[0.53; 0.97]<br>0.030<br>AD: n.a. |
| Cohort in China | 61 | n. a. [3.9; n. c.]<br>*26 (42.6)* | 62 | n.a.<br>*22 (35.5)* | 1.11<br>[0.63; 1.99]<br>0.714 |
| Total[c,d] | 325 | n. a. [21.6; n. c.]<br>*110 (33.8)* | 327 | n.a.<br>*119 (36.4)* | 0.78<br>[0.60; 1.02]<br>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.]<br>*9 (24.3)* | 37 | 3.0 [1.5; n. a.]<br>*19 (51.4)* | 0.35<br>[0.14; 0.77]<br>0.009<br>AD: n.a. |
| No presence of brain metastases at the start of the study | | | | | |
| | 288 | n. a. [21.6; n. c.]<br>*101 (35.1)* | 299 | n.a.<br>*100 (34.5)* | 0.87<br>[0.65; 1.15]<br>0.320 |
| Total | | | | Interaction: | 0.030 |

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

| Endpoint | Durvalumab + chemotherapy[a] | | Chemotherapy[a] | | Intervention vs control |
|---|---|---|---|---|---|
| | N | Median time to event in months [95% CI]<br>*Patients with event n (%)* | N | Median time to event in months [95% CI]<br>*Patients with event n (%)* | Hazard ratio [95% CI]<br>p value<br>Absolute difference (AD)[b] |
| **Immune-mediated serious adverse events [k]** | | | | | |
| Global cohort | 265 | n.a.<br>*12 (4.5)* | 266 | n.a.<br>*6 (2.3)* | 1.54<br>[0.57; 4.56]<br>0.340 |
| Cohort in China | 61 | n.a.<br>*2 (3.3)* | 62 | n.a.<br>*0 (0)* | n. d.[m] |
| Total[c,d] | 325 | n.a.<br>*14 (4.3)* | 327 | n.a.<br>*6 (1.8)* | 1.87<br>[0.72; 5.41]<br>0.120 |
| Effect modification by the feature “Gender“ | | | | | |
| Male | | | | | |
| | 240 | n.a.<br>*8 (3.3)* | 232 | n.a.<br>*6 (2.6)* | 1.15<br>[0.39; 3.52]<br>0.797 |
| Female | | | | | |
| | 85 | n.a.<br>*6 (7.1)* | 95 | n.a.<br>*0 (0)* | n. c.<br>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.<br>*8 (3.0)* | 266 | n.a.<br>*1 (0.4)* | 7.77<br>[1.42; 144.07]<br>0.014<br>AD: n.a. |
| Cohort in China | 61 | n.a.<br>*3 (4.9)* | 62 | n.a.<br>*1 (1.6)* | 3.13<br>[0.40; 63.22]<br>0.287 |
| Total[c,d] | 325 | n.a.<br>*11 (3.4)* | 327 | n.a.<br>*2 (0.6)* | 5.46<br>[1.47; 35.28]<br>0.009<br>AD: n.a. |

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

| Endpoint | Durvalumab + chemotherapy[a] | | Chemotherapy[a] | | Intervention vs control |
|---|---|---|---|---|---|
| | N | Median time to event in months [95% CI]<br>*Patients with event n (%)* | N | Median time to event in months [95% CI]<br>*Patients with event n (%)* | Hazard ratio [95% CI]<br>p value<br>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 |

**II. The resolution will enter into force on the day of its publication on the internet on the website of the G-BA on 1 April 2021.**

The justification for this resolution will be published on the G-BA website www.g-ba.de.

Berlin, 1 April 2021

Federal Joint Committee in accordance with Section 91 SGB V

The chair

Prof. Hecken