

## **Dossier zur Nutzenbewertung gemäß § 35a SGB V**

*Lurbinectedin (Zepzelca®)*

Pharma Mar S.A.

### **Modul 4A – Anhang 4G**

*Erhaltungstherapie bei erwachsenen Patienten mit  
kleinzelligem Lungenkarzinom im extensiven Stadium, deren  
Erkrankung nach einer Erstlinien-Induktionstherapie mit  
Atezolizumab, Carboplatin und Etoposid keine  
Krankheitsprogression aufweist*

Medizinischer Nutzen und  
medizinischer Zusatznutzen,  
Patientengruppen mit therapeutisch  
bedeutsamem Zusatznutzen

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**1 Unerwünschte Ereignisse (Primärer Datenschnitt 29 Juli 2024)**

Tabelle 1: Safety outcomes (dichotomous): lurbinectedin + atezolizumab vs. atezolizumab (IMforte)

| Time point<br>Outcome<br>Analysis                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               | Lurbinectedin +<br>atezolizumab |                              | Atezolizumab |                              | Lurbinectedin + atezolizumab vs. atezolizumab      |                                                    |                                                    |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------|------------------------------|--------------|------------------------------|----------------------------------------------------|----------------------------------------------------|----------------------------------------------------|
|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 | N                               | Patients with<br>event n (%) | N            | Patients with<br>event n (%) | RR [95% CI] <sup>a,b</sup><br>p-value <sup>c</sup> | RD [95% CI] <sup>a,b</sup><br>p-value <sup>c</sup> | OR [95% CI] <sup>a,b</sup><br>p-value <sup>c</sup> |
| Total AE                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        | 242                             | 235 (97.1)                   | 240          | 194 (80.8)                   | 1.20 [1.13; 1.28]<br><.0001                        | 16.27 [10.87; 21.68]<br><.0001                     | 7.96 [3.51; 18.03]<br><.0001                       |
| Severe AE<br>[CTCAE]                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |                                 |                              |              |                              |                                                    |                                                    |                                                    |
| Grade ≥3                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        | 242                             | 104 (43.0)                   | 240          | 59 (24.6)                    | 1.75 [1.34; 2.28]<br><.0001                        | 18.39 [10.11; 26.67]<br><.0001                     | 2.31 [1.57; 3.41]<br><.0001                        |
| Grade 5 (death)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 | 242                             | 12 (5.0)                     | 240          | 6 (2.5)                      | 1.98 [0.76; 5.20]<br>0.1636                        | 2.46 [-0.92; 5.83]<br>0.1532                       | 2.04 [0.75; 5.51]<br>0.1550                        |
| Serious AE                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | 242                             | 75 (31.0)                    | 240          | 41 (17.1)                    | 1.81 [1.30; 2.54]<br>0.0005                        | 13.91 [6.38; 21.43]<br>0.0003                      | 2.18 [1.41; 3.36]<br>0.0004                        |
| Treatment<br>discontinuation<br>due to AE                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       | 242                             | 15 (6.2)                     | 240          | 8 (3.3)                      | 1.86 [0.80; 4.30]<br>0.1475                        | 2.87 [-0.93; 6.66]<br>0.1388                       | 1.92 [0.80; 4.61]<br>0.1405                        |
| Immune-related<br>AE <sup>d</sup>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               | 242                             | 75 (31.0)                    | 240          | 54 (22.5)                    | 1.38 [1.02; 1.86]<br>0.0369                        | 8.49 [0.21; 16.77]<br>0.0402                       | 1.55 [1.03; 2.32]<br>0.0354                        |
| Reading the “Hypothesis testing” columns:<br>1: Statistical significance: S = Statistically significant against the alpha level specified in the statistical analysis plan of the corresponding study or protocol for evidence synthesis NS = Non-significant, NO = Nominal p-value<br>2: Prespecification: P = Statistical test was prespecified according to the statistical analysis plan of the corresponding study, NP = Not prespecified<br>3: Multiple hypothesis testing. C = Appropriate control for multiplicity according to the statistical analysis plan and clinical study report of the corresponding study, NC = Not controlled |                                 |                              |              |                              |                                                    |                                                    |                                                    |

| Time point<br>Outcome                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | Lurbinectedin +<br>atezolizumab |                              | Atezolizumab |                              | Lurbinectedin + atezolizumab vs. atezolizumab      |                                                    |                                                    |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------|------------------------------|--------------|------------------------------|----------------------------------------------------|----------------------------------------------------|----------------------------------------------------|
| Analysis                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   | N                               | Patients with<br>event n (%) | N            | Patients with<br>event n (%) | RR [95% CI] <sup>a,b</sup><br>p-value <sup>c</sup> | RD [95% CI] <sup>a,b</sup><br>p-value <sup>c</sup> | OR [95% CI] <sup>a,b</sup><br>p-value <sup>c</sup> |
| CCOD: 29 July 2024                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |                                 |                              |              |                              |                                                    |                                                    |                                                    |
| a: estimates were derived using the Mantel-Haenszel method on 2x2 contingency table with the stratification factors ECOG PS at randomization (0 vs. 1), LDH at randomization ( $\leq$ ULN vs $>$ ULN) via local laboratory test, presence of liver metastases at enrollment (yes vs. no), and prior receipt of PCI (yes vs. no).                                                                                                                                                                                                                                                                                           |                                 |                              |              |                              |                                                    |                                                    |                                                    |
| b: 95% CI were constructed using the Wald method (normal approximation to the binomial distribution) with continuity correction.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |                                 |                              |              |                              |                                                    |                                                    |                                                    |
| c: p-value were calculated using a stratified Mantel-Haenszel test. The stratification factors are ECOG PS at randomization (0 vs. 1), LDH at randomization ( $\leq$ ULN vs $>$ ULN) via local laboratory test, presence of liver metastases at enrollment (yes vs. no), and prior receipt of PCI (yes vs. no).                                                                                                                                                                                                                                                                                                            |                                 |                              |              |                              |                                                    |                                                    |                                                    |
| d: specific AE, as requested by the assessment scope. Immune-related AE were calculated as a combined endpoint comprising the following immune-mediated AE: adrenal insufficiency, colitis, diabetes mellitus, encephalitis, Guillain-Barre syndrome, hepatitis (diagnosis and lab abnormalities), hepatitis (diagnosis), hepatitis (lab abnormalities), hyperthyroidism, hypothyroidism, meningoencephalitis, myositis, myositis (myositis + rhabdomyolysis) nephritis, ocular inflammatory toxicity, pancreatitis, pericardial disorders, pneumonitis, rhabdomyolysis, rash, severe cutaneous reactions, and vasculitis. |                                 |                              |              |                              |                                                    |                                                    |                                                    |

Tabelle 2: Safety outcomes (time-to-event): lurbinectedin + atezolizumab vs. atezolizumab (IMforte)

| Time point<br>Outcome | Lurbinectedin + atezolizumab |                                                                                                    | Atezolizumab       |                                                                                                    | Lurbinectedin + atezolizumab vs. atezolizumab    |
|-----------------------|------------------------------|----------------------------------------------------------------------------------------------------|--------------------|----------------------------------------------------------------------------------------------------|--------------------------------------------------|
| Analysis              | N/N <sup>Cen</sup>           | Median time to event in days <sup>a</sup><br>[95% CI] <sup>b</sup><br>patients with event<br>n (%) | N/N <sup>Cen</sup> | Median time to event in days <sup>a</sup><br>[95% CI] <sup>b</sup><br>patients with event<br>n (%) | HR [95% CI] <sup>c</sup><br>p-value <sup>d</sup> |
| Total AE              | 242/7                        | 10 [9; 11]<br>235 (97.1)                                                                           | 240/46             | 35 [24; 43]<br>194 (80.8)                                                                          | 2.18 [1.79; 2.66]<br><.0001                      |
| Severe AE<br>[CTCAE]  |                              |                                                                                                    |                    |                                                                                                    |                                                  |

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

| Time point<br>Outcome<br>Analysis                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             | Lurbinectedin + atezolizumab |                                                                                                    | Atezolizumab       |                                                                                                    | Lurbinectedin + atezolizumab vs. atezolizumab    |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------|----------------------------------------------------------------------------------------------------|--------------------|----------------------------------------------------------------------------------------------------|--------------------------------------------------|
|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               | N/N <sup>Cen</sup>           | Median time to event in days <sup>a</sup><br>[95% CI] <sup>b</sup><br>patients with event<br>n (%) | N/N <sup>Cen</sup> | Median time to event in days <sup>a</sup><br>[95% CI] <sup>b</sup><br>patients with event<br>n (%) | HR [95% CI] <sup>c</sup><br>p-value <sup>d</sup> |
| Grade ≥3                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | 242/138                      | 343 [254; 393]<br>104 (43.0)                                                                       | 240/181            | NE [NE; NE]<br>59 (24.6)                                                                           | 1.75 [1.27; 2.41]<br>0.0006                      |
| Grade 5<br>(death)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            | 242/230                      | NE [NE; NE]<br>12 (5.0)                                                                            | 240/234            | NE [NE; NE]<br>6 (2.5)                                                                             | 1.64 [0.61; 4.41]<br>0.3218                      |
| Serious AE                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | 242/167                      | NE [399; NE]<br>75 (31.0)                                                                          | 240/199            | NE [NE; NE]<br>41 (17.1)                                                                           | 1.71 [1.17; 2.51]<br>0.0054                      |
| Treatment<br>discontinuation due<br>to AE                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | 242/227                      | NE [NE; NE]<br>15 (6.2)                                                                            | 240/232            | NE [NE; NE]<br>8 (3.3)                                                                             | 1.62 [0.69; 3.85]<br>0.2667                      |
| Immune-related<br>AE <sup>e</sup>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             | 242/167                      | 444 [324; NE]<br>75 (31.0)                                                                         | 240/186            | NE [NE; NE]<br>54 (22.5)                                                                           | 1.27 [0.89; 1.81]<br>0.1876                      |
| Reading the “Hypothesis testing” columns:<br>1. Statistical significance: S = Statistically significant against the alpha level specified in the statistical analysis plan of the corresponding study, NS = Non-significant, NO = Nominal p-value<br>2. Prespecification: P = Statistical test was prespecified according to the statistical analysis plan of the corresponding study, NP = Not prespecified<br>3. Multiple hypothesis testing. C = Appropriate control for multiplicity according to the statistical analysis plan and clinical study report of the corresponding study, NC = Not controlled |                              |                                                                                                    |                    |                                                                                                    |                                                  |

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

| Time point                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               | Lurbinectedin + atezolizumab |                                                                                                    | Atezolizumab       |                                                                                                    | Lurbinectedin + atezolizumab vs. atezolizumab    |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------|----------------------------------------------------------------------------------------------------|--------------------|----------------------------------------------------------------------------------------------------|--------------------------------------------------|
| Outcome                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  | N/N <sup>Cen</sup>           | Median time to event in days <sup>a</sup><br>[95% CI] <sup>b</sup><br>patients with event<br>n (%) | N/N <sup>Cen</sup> | Median time to event in days <sup>a</sup><br>[95% CI] <sup>b</sup><br>patients with event<br>n (%) | HR [95% CI] <sup>c</sup><br>p-value <sup>d</sup> |
| Analysis                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |                              |                                                                                                    |                    |                                                                                                    |                                                  |
| <p>CCOD: 29 July 2024; NE: not estimable.</p> <p>a: summaries of duration (median) are Kaplan-Meier estimates.</p> <p>b: 95% CIs for the median were computed using the method of Brookmeyer and Crowley.</p> <p>c: hazard ratios were estimated using a stratified Cox proportional hazard model. The stratification factors are ECOG PS at randomization (0 vs. 1), LDH at randomization (<math>\leq</math>ULN vs <math>&gt;</math>ULN) via local laboratory test, presence of liver metastases at enrollment (yes vs. no), and prior receipt of PCI (yes vs. no).</p> <p>d: p-value based on the log rank test.</p> <p>e: specific AE, as requested by the assessment scope. Immune-related AE were calculated as a combined endpoint comprising the following immune-mediated AE: adrenal insufficiency, colitis, diabetes mellitus, encephalitis, Guillain-Barre syndrome, hepatitis (diagnosis and lab abnormalities), hepatitis (diagnosis), hepatitis (lab abnormalities), hyperthyroidism, hypothyroidism, meningoencephalitis, myositis, myositis (myositis + rhabdomyolysis) nephritis, ocular inflammatory toxicity, pancreatitis, pericardial disorders, pneumonitis, rhabdomyolysis, rash, severe cutaneous reactions, and vasculitis.</p> |                              |                                                                                                    |                    |                                                                                                    |                                                  |

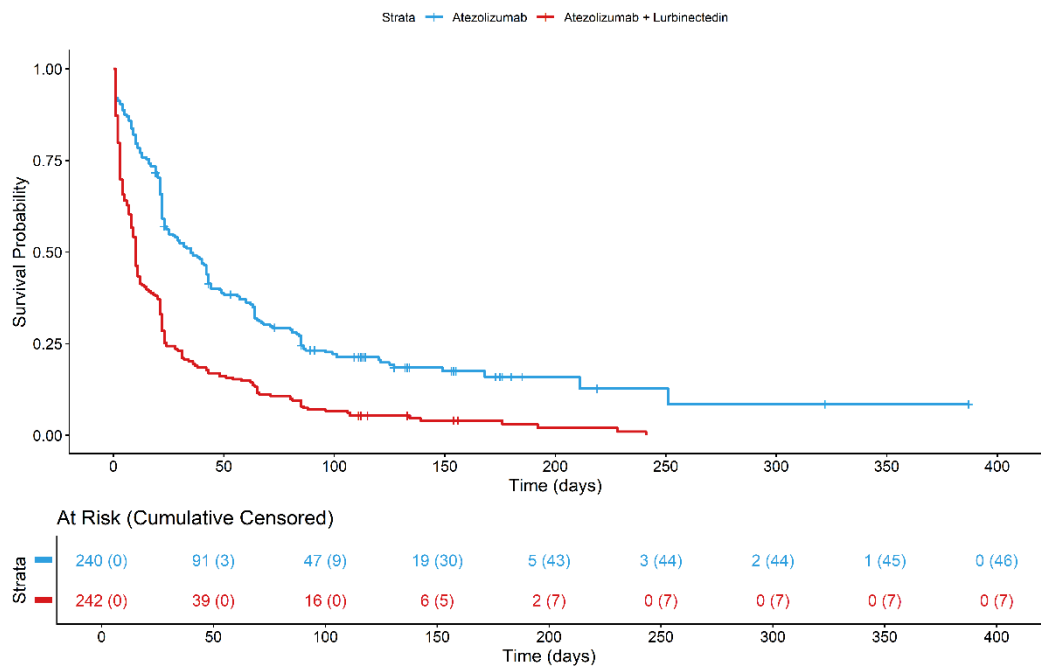


Abbildung 1: Kaplan-Meier plot for total AE, IMforte trial, Safety Analysis Set, CCOD 29 July 2024

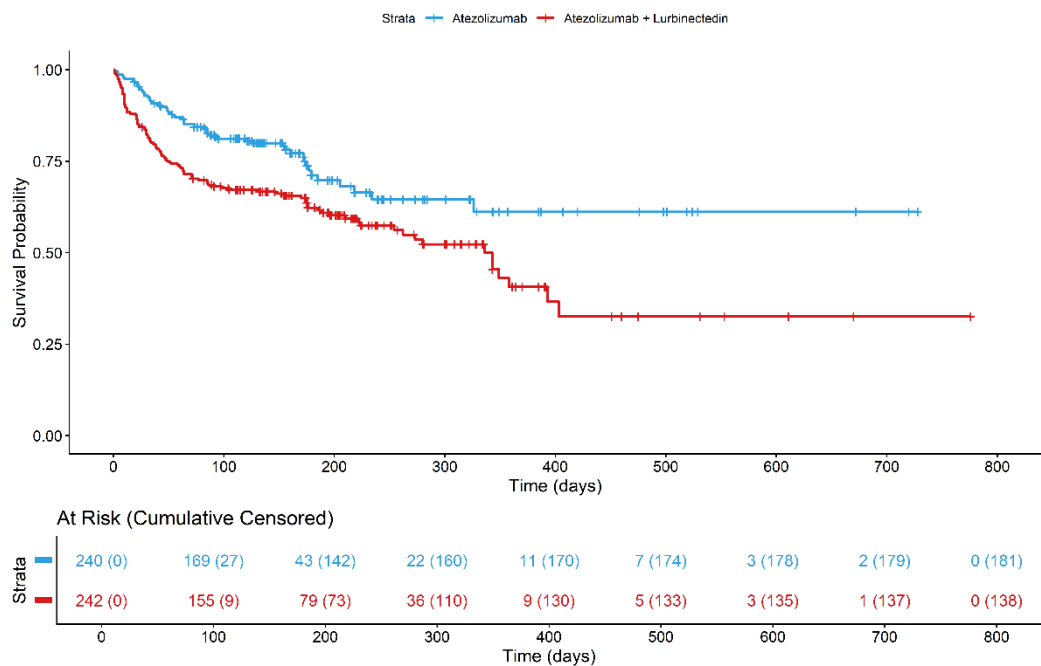


Abbildung 2: Kaplan-Meier plot for severe AE, IMforte trial, Safety Analysis Set, CCOD 29 July 2024

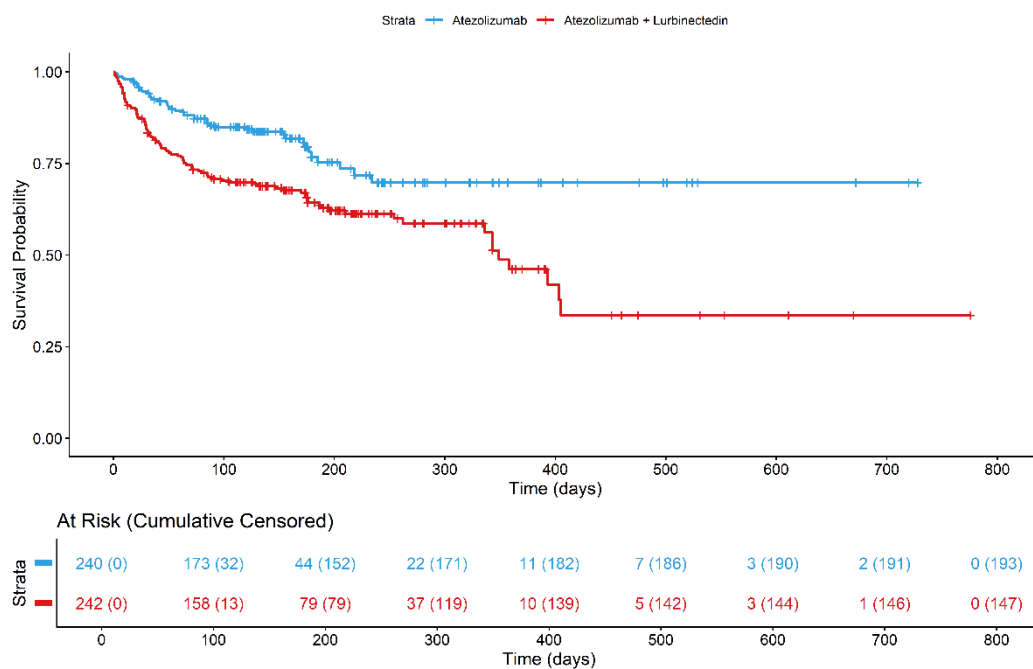


Abbildung 3: Kaplan-Meier plot for grade 3 AE, IMforte trial, Safety Analysis Set, CCOD 29 July 2024

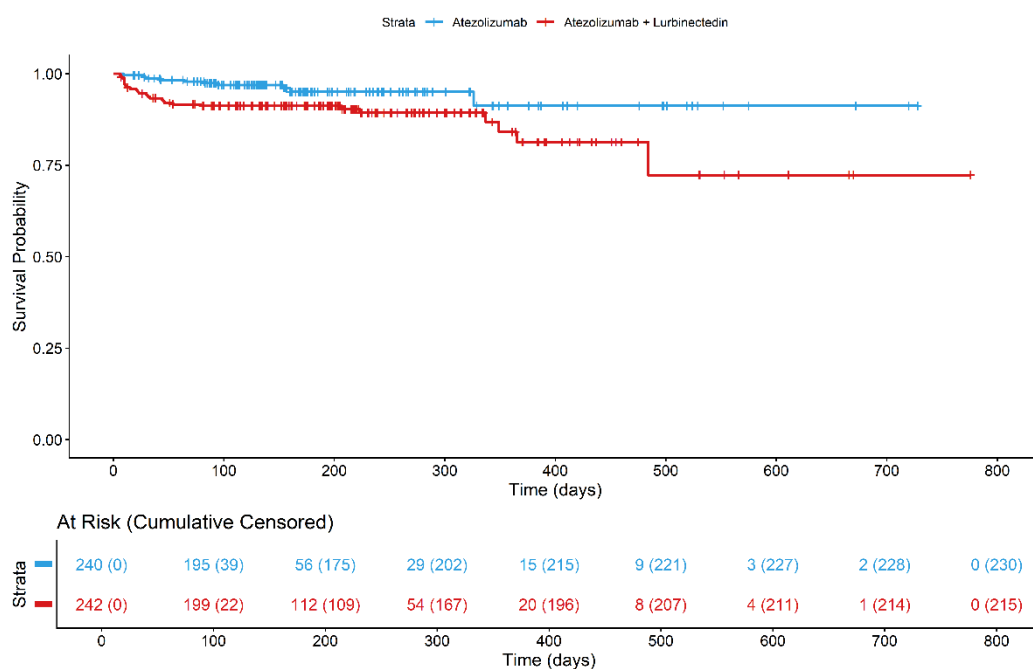


Abbildung 4: Kaplan-Meier plot for grade 4 AE, IMforte trial, Safety Analysis Set, CCOD 29 July 2024

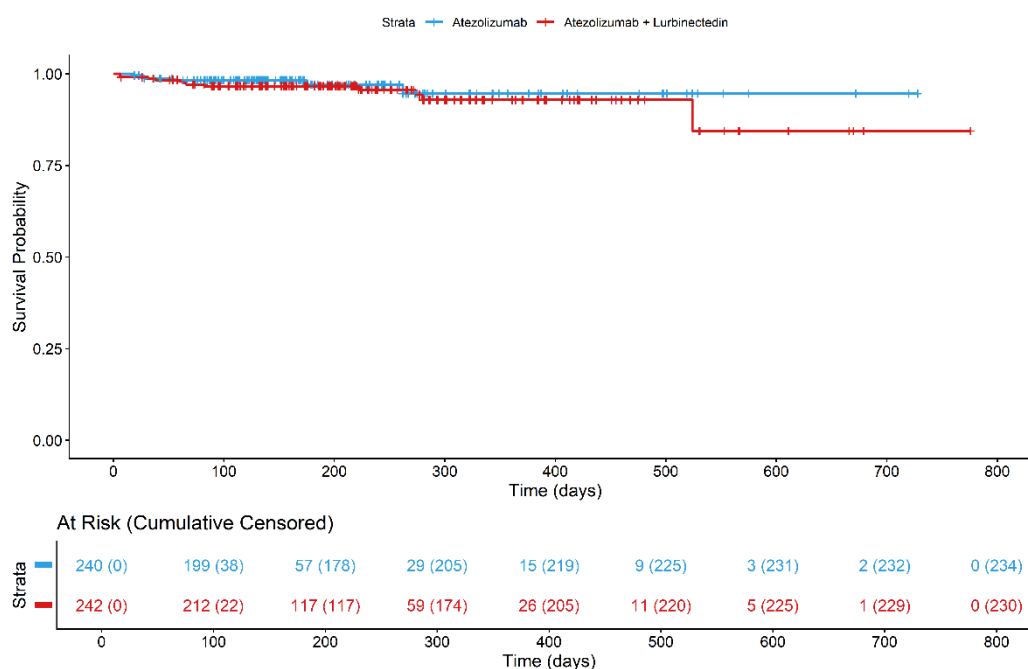


Abbildung 5: Kaplan-Meier plot for grade 5 AE, IMforte trial, Safety Analysis Set, CCOD 29 July 2024

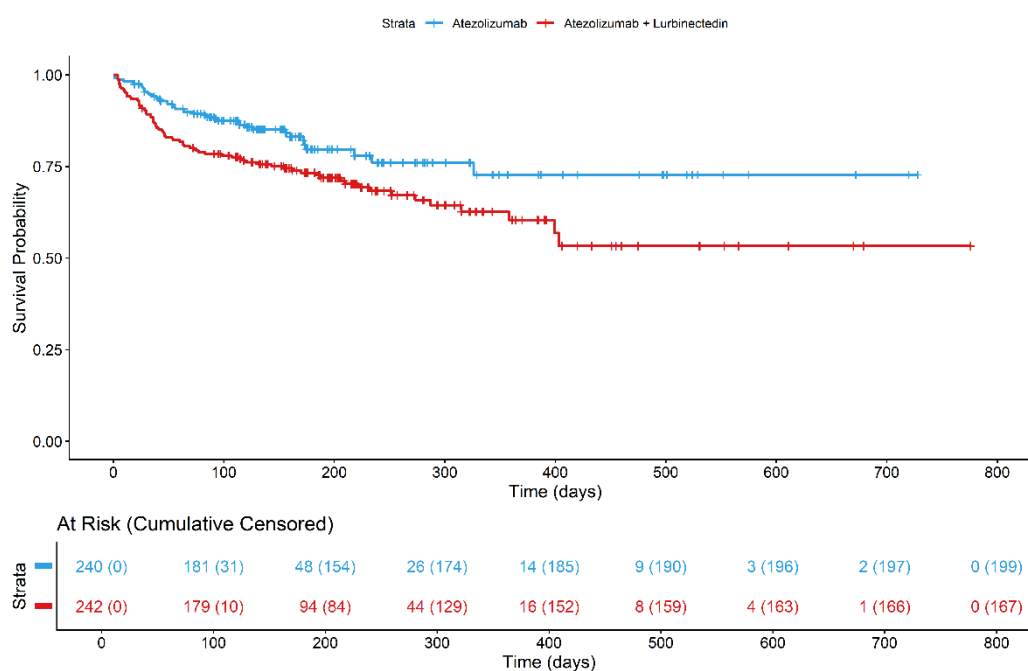


Abbildung 6: Kaplan-Meier plot for serious AE, IMforte trial, Safety Analysis Set, CCOD 29 July 2024

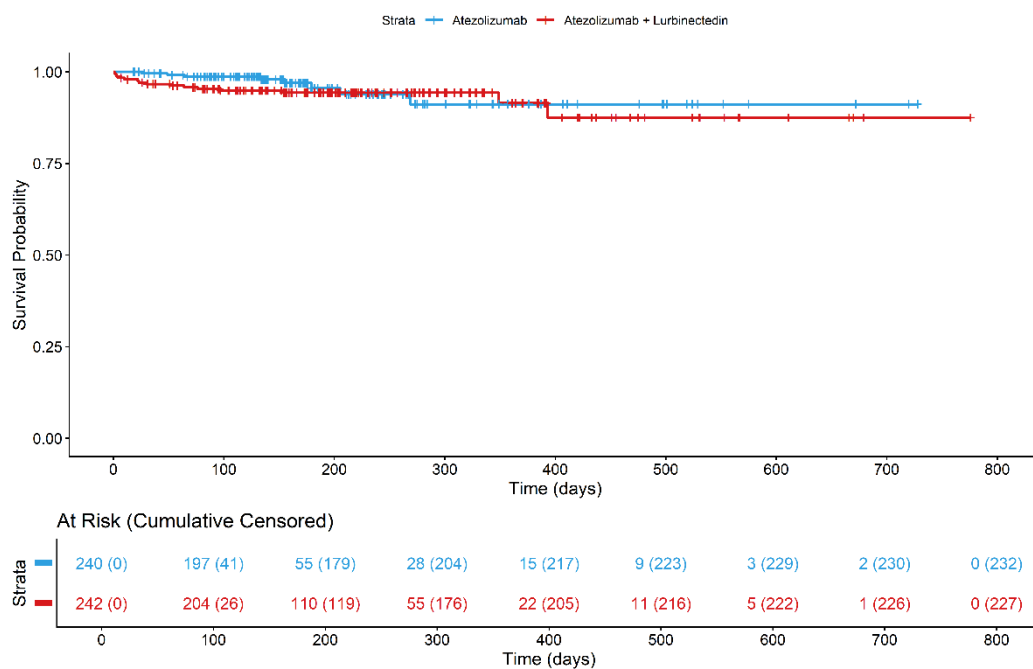


Abbildung 7: Kaplan-Meier plot for treatment discontinuation due to AE, IMforte trial, Safety Analysis Set, CCOD 29 July 2024

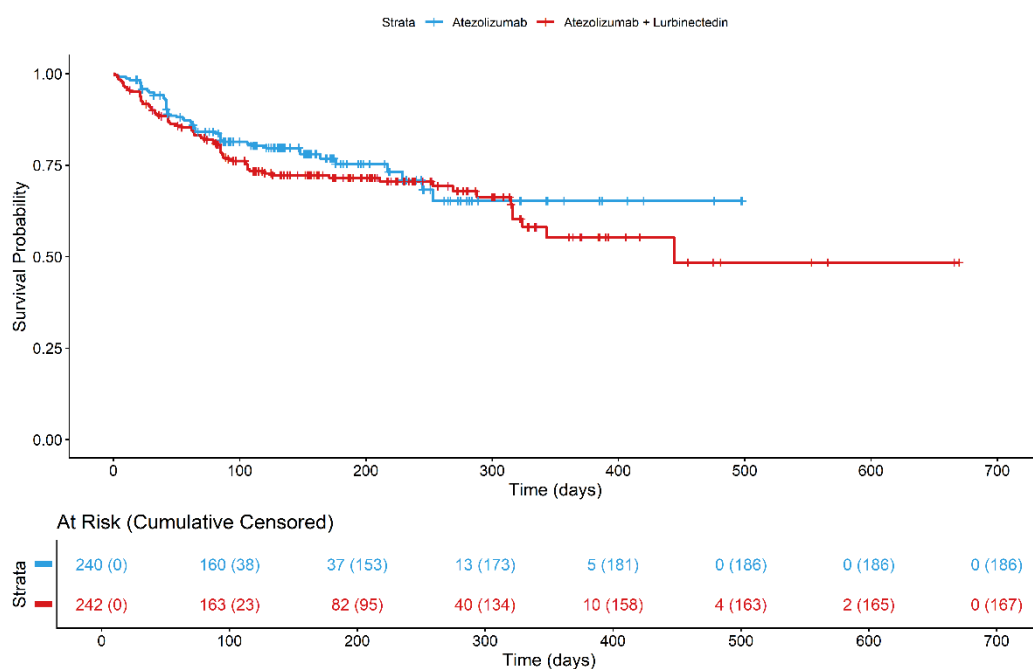


Abbildung 8: Kaplan-Meier plot for any immune-related AE, IMforte trial, Safety Analysis Set, CCOD 29 July 2024

Tabelle 3: AE of any severity by SOC and PT including effect estimates

| Endpoint<br>SOC<br>PT                   | Lurbinectedin + atezolizumab |                                                                                                       | Atezolizumab       |                                                                                                    | Lurbinectedin + atezolizumab vs.<br>atezolizumab |
|-----------------------------------------|------------------------------|-------------------------------------------------------------------------------------------------------|--------------------|----------------------------------------------------------------------------------------------------|--------------------------------------------------|
|                                         | N/N <sup>Cen</sup>           | Median time to<br>event in days <sup>a</sup><br>[95% CI] <sup>b</sup><br>patients with event<br>n (%) | N/N <sup>Cen</sup> | Median time to event in days <sup>a</sup><br>[95% CI] <sup>b</sup><br>patients with event<br>n (%) | HR [95% CI] <sup>c</sup><br>p-value <sup>d</sup> |
| Blood and lymphatic<br>system disorders | 242/141                      | 343 [246; 400]<br>101 (41.7)                                                                          | 240/218            | NE [NE; NE]<br>22 (9.2)                                                                            | 5.21 [3.28; 8.26]<br><.0001                      |
| Anemia                                  | 242/165                      | 400 [349; NE]<br>77 (31.8)                                                                            | 240/224            | NE [NE; NE]<br>16 (6.7)                                                                            | 5 [2.91; 8.55]<br><.0001                         |
| Neutropenia                             | 242/216                      | NE [NE; NE]<br>26 (10.7)                                                                              | 240/236            | NE [NE; NE]<br>4 (1.7)                                                                             | 6.17 [2.16; 7.86]<br><.0001                      |
| Thrombocytopenia                        | 242/211                      | NE [NE; NE]<br>31 (12.8)                                                                              | 240/236            | NE [NE; NE]<br>4 (1.7)                                                                             | 7.63 [2.70; 21.74]<br><.0001                     |
| Cardiac disorders                       | 242/228                      | NE [NE; NE]<br>14 (5.8)                                                                               | 240/236            | NE [NE; NE]<br>4 (1.7)                                                                             | 3.09 [1.01; 9.43]<br>0.0368                      |
| Endocrine disorders                     | 242/217                      | NE [NE; NE]<br>25 (10.3)                                                                              | 240/216            | NE [NE; NE]<br>24 (10.0)                                                                           | 0.95 [0.54; 1.66]<br>0.8451                      |
| Hypothyroidism                          | 242/225                      | NE [NE; NE]<br>17 (7.0)                                                                               | 240/223            | NE [NE; NE]<br>17 (7.1)                                                                            | 0.89 [0.45; 1.75]<br>0.7390                      |
| Gastrointestinal<br>disorders           | 242/102                      | 85 [44; 157]<br>140 (57.9)                                                                            | 240/180            | NE [420; NE]<br>60 (25.0)                                                                          | 3.06 [2.25; 4.15]<br><.0001                      |
| Abdominal pain                          | 242/230                      | NE [NE; NE]<br>12 (5.0)                                                                               | 240/236            | NE [NE; NE]<br>4 (1.7)                                                                             | 2.70 [0.87; 8.40]<br>0.0736                      |

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

| Endpoint<br>SOC<br>PT                                      | Lurbinectedin + atezolizumab |                                                                                                       | Atezolizumab       |                                                                                                    | Lurbinectedin + atezolizumab vs.<br>atezolizumab |
|------------------------------------------------------------|------------------------------|-------------------------------------------------------------------------------------------------------|--------------------|----------------------------------------------------------------------------------------------------|--------------------------------------------------|
|                                                            | N/N <sup>Cen</sup>           | Median time to<br>event in days <sup>a</sup><br>[95% CI] <sup>b</sup><br>patients with event<br>n (%) | N/N <sup>Cen</sup> | Median time to event in days <sup>a</sup><br>[95% CI] <sup>b</sup><br>patients with event<br>n (%) | HR [95% CI] <sup>c</sup><br>p-value <sup>d</sup> |
| Constipation                                               | 242/213                      | NE [NE; NE]<br>29 (12.0)                                                                              | 240/225            | NE [NE; NE]<br>15 (6.3)                                                                            | 1.79 [0.96; 3.34]<br>0.0649                      |
| Diarrhea                                                   | 242/208                      | NE [NE; NE]<br>34 (14.0)                                                                              | 240/222            | NE [NE; NE]<br>18 (7.5)                                                                            | 1.76 [0.99; 3.14]<br>0.0496                      |
| Nausea                                                     | 242/154                      | NE [NE; NE]<br>88 (36.4)                                                                              | 240/230            | NE [NE; NE]<br>10 (4.2)                                                                            | 10.42 [5.38; 0]<br><.0001                        |
| Vomiting                                                   | 242/209                      | NE [NE; NE]<br>33 (13.6)                                                                              | 240/234            | NE [NE; NE]<br>6 (2.5)                                                                             | 5.53 [2.32; 13.16]<br><.0001                     |
| General disorders and<br>administration site<br>conditions | 242/129                      | 263 [170; 434]<br>113 (46.7)                                                                          | 240/176            | 610 [610; NE]<br>64 (26.7)                                                                         | 1.92 [1.41; 2.60]<br><.0001                      |
| Asthenia                                                   | 242/211                      | NE [NE; NE]<br>31 (12.8)                                                                              | 240/225            | NE [NE; NE]<br>15 (6.3)                                                                            | 1.87 [1.01; 3.48]<br>0.0442                      |
| Chest pain                                                 | 242/236                      | NE [NE; NE]<br>6 (2.5)                                                                                | 240/228            | NE [NE; NE]<br>12 (5.0)                                                                            | 0.43 [0.16; 1.16]<br>0.0882                      |
| Fatigue                                                    | 242/193                      | NE [NE; NE]<br>49 (20.2)                                                                              | 240/221            | NE [NE; NE]<br>19 (7.9)                                                                            | 2.57 [1.51; 4.37]<br>0.0003                      |
| Oedema peripheral                                          | 242/230                      | NE [NE; NE]<br>12 (5.0)                                                                               | 240/236            | NE [NE; NE]<br>4 (1.7)                                                                             | 2.61 [0.84; 8.13]<br>0.0860                      |

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

| Endpoint<br>SOC<br>PT                                | Lurbinectedin + atezolizumab |                                                                                                       | Atezolizumab       |                                                                                                    | Lurbinectedin + atezolizumab vs.<br>atezolizumab |
|------------------------------------------------------|------------------------------|-------------------------------------------------------------------------------------------------------|--------------------|----------------------------------------------------------------------------------------------------|--------------------------------------------------|
|                                                      | N/N <sup>Cen</sup>           | Median time to<br>event in days <sup>a</sup><br>[95% CI] <sup>b</sup><br>patients with event<br>n (%) | N/N <sup>Cen</sup> | Median time to event in days <sup>a</sup><br>[95% CI] <sup>b</sup><br>patients with event<br>n (%) | HR [95% CI] <sup>c</sup><br>p-value <sup>d</sup> |
| Pyrexia                                              | 242/229                      | NE [NE; NE]<br>13 (5.4)                                                                               | 240/238            | NE [NE; NE]<br>2 (0.8)                                                                             | 6.10 [1.37; 7.03]<br>0.0069                      |
| Infections and<br>infestations                       | 242/151                      | 357 [303; 427]<br>91 (37.6)                                                                           | 240/179            | 539 [328; NE]<br>61 (25.4)                                                                         | 1.37 [0.99; 1.90]<br>0.0571                      |
| COVID-19                                             | 242/228                      | NE [NE; NE]<br>14 (5.8)                                                                               | 240/236            | NE [NE; NE]<br>4 (1.7)                                                                             | 3.22 [1.06; 9.80]<br>0.0299                      |
| Pneumonia                                            | 242/233                      | NE [NE; NE]<br>9 (3.7)                                                                                | 240/228            | NE [NE; NE]<br>12 (5.0)                                                                            | 0.65 [0.27; 1.55]<br>0.3252                      |
| Upper respiratory<br>tract infection                 | 242/230                      | NE [NE; NE]<br>12 (5.0)                                                                               | 240/232            | NE [539; NE]<br>8 (3.3)                                                                            | 1.23 [0.50; 3.03]<br>0.6521                      |
| Urinary tract<br>infection                           | 242/230                      | NE [NE; NE]<br>12 (5.0)                                                                               | 240/236            | NE [NE; NE]<br>4 (1.7)                                                                             | 2.68 [0.86; 8.33]<br>0.0766                      |
| Injury, poisoning and<br>procedural<br>complications | 242/228                      | NE [NE; NE]<br>14 (5.8)                                                                               | 240/232            | NE [NE; NE]<br>8 (3.3)                                                                             | 1.44 [0.60; 3.45]<br>0.4129                      |
| Investigations                                       | 242/155                      | 484 [288; NE]<br>87 (36.0)                                                                            | 240/192            | NE [340; NE]<br>48 (20.0)                                                                          | 1.81 [1.27; 2.58]<br>0.0010                      |
| Alanine<br>aminotransferase<br>increased             | 242/226                      | NE [NE; NE]<br>16 (6.6)                                                                               | 240/231            | NE [NE; NE]<br>9 (3.8)                                                                             | 1.64 [0.72; 3.73]<br>0.2317                      |

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

| Endpoint<br>SOC<br>PT                          | Lurbinectedin + atezolizumab |                                                                                                       | Atezolizumab       |                                                                                                    | Lurbinectedin + atezolizumab vs.<br>atezolizumab |
|------------------------------------------------|------------------------------|-------------------------------------------------------------------------------------------------------|--------------------|----------------------------------------------------------------------------------------------------|--------------------------------------------------|
|                                                | N/N <sup>Cen</sup>           | Median time to<br>event in days <sup>a</sup><br>[95% CI] <sup>b</sup><br>patients with event<br>n (%) | N/N <sup>Cen</sup> | Median time to event in days <sup>a</sup><br>[95% CI] <sup>b</sup><br>patients with event<br>n (%) | HR [95% CI] <sup>c</sup><br>p-value <sup>d</sup> |
| Aspartate<br>aminotransferase<br>increased     | 242/226                      | NE [NE; NE]<br>16 (6.6)                                                                               | 240/229            | NE [NE; NE]<br>11 (4.6)                                                                            | 1.25 [0.58; 2.71]<br>0.5749                      |
| Blood creatinine<br>phosphokinase<br>increased | 242/238                      | NE [NE; NE]<br>4 (1.7)                                                                                | 240/228            | NE [NE; NE]<br>12 (5.0)                                                                            | 0.27 [0.09; 0.85]<br>0.0162                      |
| Blood creatinine<br>increased                  | 242/229                      | NE [NE; NE]<br>13 (5.4)                                                                               | 240/237            | NE [NE; NE]<br>3 (1.3)                                                                             | 3.92 [1.12; 3.89]<br>0.0216                      |
| Lymphocyte count<br>decreased                  | 242/232                      | NE [NE; NE]<br>10 (4.1)                                                                               | 240/234            | NE [NE; NE]<br>6 (2.5)                                                                             | 1.51 [0.55; 4.17]<br>0.4237                      |
| Neutrophil count<br>decreased                  | 242/211                      | NE [NE; NE]<br>31 (12.8)                                                                              | 240/237            | NE [NE; NE]<br>3 (1.3)                                                                             | 9.80 [2.99; 32.26]<br><.0001                     |
| Platelet count<br>decreased                    | 242/205                      | NE [NE; NE]<br>37 (15.3)                                                                              | 240/233            | NE [NE; NE]<br>7 (2.9)                                                                             | 5.16 [2.29; 11.63]<br><.0001                     |
| White blood cell<br>count decreased            | 242/223                      | NE [NE; NE]<br>19 (7.9)                                                                               | 240/235            | NE [NE; NE]<br>5 (2.1)                                                                             | 3.47 [1.29; 9.35]<br>0.0087                      |
| Metabolism and<br>nutrition disorders          | 242/157                      | NE [393; NE]<br>85 (35.1)                                                                             | 240/184            | NE [466; NE]<br>56 (23.3)                                                                          | 1.57 [1.12; 2.21]<br>0.0085                      |
| Decreased appetite                             | 242/201                      | NE [NE; NE]<br>41 (16.9)                                                                              | 240/224            | NE [NE; NE]<br>16 (6.7)                                                                            | 2.56 [1.43; 4.57]<br>0.0010                      |

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

| Endpoint<br>SOC<br>PT                           | Lurbinectedin + atezolizumab |                                                                                                    | Atezolizumab       |                                                                                                    | Lurbinectedin + atezolizumab vs.<br>atezolizumab |
|-------------------------------------------------|------------------------------|----------------------------------------------------------------------------------------------------|--------------------|----------------------------------------------------------------------------------------------------|--------------------------------------------------|
|                                                 | N/N <sup>Cen</sup>           | Median time to event in days <sup>a</sup><br>[95% CI] <sup>b</sup><br>patients with event<br>n (%) | N/N <sup>Cen</sup> | Median time to event in days <sup>a</sup><br>[95% CI] <sup>b</sup><br>patients with event<br>n (%) | HR [95% CI] <sup>c</sup><br>p-value <sup>d</sup> |
| Hypomagnesaemia                                 | 242/230                      | NE [NE; NE]<br>12 (5.0)                                                                            | 240/235            | NE [NE; NE]<br>5 (2.1)                                                                             | 2.32 [0.81; 6.58]<br>0.1058                      |
| Hyponatremia                                    | 242/231                      | NE [NE; NE]<br>11 (4.5)                                                                            | 240/226            | NE [NE; NE]<br>14 (5.8)                                                                            | 0.65 [0.29; 1.43]<br>0.2778                      |
| Musculoskeletal and connective tissue disorders | 242/188                      | NE [NE; NE]<br>54 (22.3)                                                                           | 240/194            | 523 [523; NE]<br>46 (19.2)                                                                         | 1.08 [0.73; 1.60]<br>0.7105                      |
| Arthralgia                                      | 242/222                      | NE [NE; NE]<br>20 (8.3)                                                                            | 240/228            | NE [538; NE]<br>12 (5.0)                                                                           | 1.42 [0.69; 2.91]<br>0.3407                      |
| Back pain                                       | 242/229                      | NE [NE; NE]<br>13 (5.4)                                                                            | 240/231            | NE [NE; NE]<br>9 (3.8)                                                                             | 1.35 [0.58; 3.18]<br>0.4870                      |
| Myalgia                                         | 242/230                      | NE [NE; NE]<br>12 (5.0)                                                                            | 240/236            | NE [NE; NE]<br>4 (1.7)                                                                             | 2.78 [0.89; 8.62]<br>0.0657                      |
| Nervous system disorders                        | 242/183                      | 413 [393; NE]<br>59 (24.4)                                                                         | 240/203            | NE [NE; NE]<br>37 (15.4)                                                                           | 1.37 [0.91; 2.08]<br>0.1324                      |
| Dizziness                                       | 242/225                      | NE [NE; NE]<br>17 (7.0)                                                                            | 240/235            | NE [NE; NE]<br>5 (2.1)                                                                             | 2.77 [1.02; 7.58]<br>0.0376                      |
| Headache                                        | 242/227                      | NE [NE; NE]<br>15 (6.2)                                                                            | 240/234            | NE [NE; NE]<br>6 (2.5)                                                                             | 2.10 [0.81; 5.46]<br>0.1179                      |

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

| Endpoint<br>SOC<br>PT                                 | Lurbinectedin + atezolizumab |                                                                                                       | Atezolizumab       |                                                                                                    | Lurbinectedin + atezolizumab vs.<br>atezolizumab |
|-------------------------------------------------------|------------------------------|-------------------------------------------------------------------------------------------------------|--------------------|----------------------------------------------------------------------------------------------------|--------------------------------------------------|
|                                                       | N/N <sup>Cen</sup>           | Median time to<br>event in days <sup>a</sup><br>[95% CI] <sup>b</sup><br>patients with event<br>n (%) | N/N <sup>Cen</sup> | Median time to event in days <sup>a</sup><br>[95% CI] <sup>b</sup><br>patients with event<br>n (%) | HR [95% CI] <sup>c</sup><br>p-value <sup>d</sup> |
| Psychiatric disorders                                 | 242/220                      | NE [NE; NE]<br>22 (9.1)                                                                               | 240/232            | NE [NE; NE]<br>8 (3.3)                                                                             | 2.36 [1.05; 5.32]<br>0.0334                      |
| Renal and urinary<br>disorders                        | 242/225                      | NE [NE; NE]<br>17 (7.0)                                                                               | 240/233            | NE [NE; NE]<br>7 (2.9)                                                                             | 2.17 [0.90; 5.26]<br>0.0780                      |
| Respiratory, thoracic<br>and mediastinal<br>disorders | 242/169                      | NE [NE; NE]<br>73 (30.2)                                                                              | 240/183            | 604 [473; NE]<br>57 (23.8)                                                                         | 1.22 [0.86; 1.73]<br>0.2589                      |
| Cough                                                 | 242/219                      | NE [NE; NE]<br>23 (9.5)                                                                               | 240/224            | NE [NE; NE]<br>16 (6.7)                                                                            | 1.32 [0.70; 2.50]<br>0.3940                      |
| Dyspnea                                               | 242/218                      | NE [NE; NE]<br>24 (9.9)                                                                               | 240/222            | NE [NE; NE]<br>18 (7.5)                                                                            | 1.22 [0.66; 2.26]<br>0.5179                      |
| Skin and<br>subcutaneous tissue<br>disorders          | 242/205                      | NE [454; NE]<br>37 (15.3)                                                                             | 240/194            | 494 [297; NE]<br>46 (19.2)                                                                         | 0.63 [0.41; 0.98]<br>0.0392                      |
| Pruritus                                              | 242/224                      | NE [NE; NE]<br>18 (7.4)                                                                               | 240/223            | NE [NE; NE]<br>17 (7.1)                                                                            | 0.82 [0.42; 1.61]<br>0.5641                      |
| Vascular disorders                                    | 242/199                      | NE [483; NE]<br>43 (17.8)                                                                             | 240/229            | NE [NE; NE]<br>11 (4.6)                                                                            | 3.72 [1.92; 7.25]<br><.0001                      |
| Phlebitis                                             | 242/226                      | NE [NE; NE]<br>16 (6.6)                                                                               | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [0.00; NE]<br><.0001                          |
| CCOD: 29 July 2024; NE: not estimable.                |                              |                                                                                                       |                    |                                                                                                    |                                                  |

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

| Endpoint<br>SOC | Lurbinectedin + atezolizumab |                                                                                                       | Atezolizumab       |                                                                                                    | Lurbinectedin + atezolizumab vs.<br>atezolizumab |
|-----------------|------------------------------|-------------------------------------------------------------------------------------------------------|--------------------|----------------------------------------------------------------------------------------------------|--------------------------------------------------|
|                 | N/N <sup>Cen</sup>           | Median time to<br>event in days <sup>a</sup><br>[95% CI] <sup>b</sup><br>patients with event<br>n (%) | N/N <sup>Cen</sup> | Median time to event in days <sup>a</sup><br>[95% CI] <sup>b</sup><br>patients with event<br>n (%) | HR [95% CI] <sup>c</sup><br>p-value <sup>d</sup> |
| PT              |                              |                                                                                                       |                    |                                                                                                    |                                                  |

a: summaries of duration (median) are Kaplan-Meier estimates.  
b: 95% CIs for the median were computed using the method of Brookmeyer and Crowley.  
c: hazard ratios were estimated using a stratified Cox proportional hazard model. The stratification factors are ECOG PS at randomization (0 vs. 1), LDH at randomization ( $\leq$ ULN vs  $>$ ULN) via local laboratory test, presence of liver metastases at enrollment (yes vs. no), and prior receipt of PCI (yes vs. no).  
d: p-value based on the log rank test.

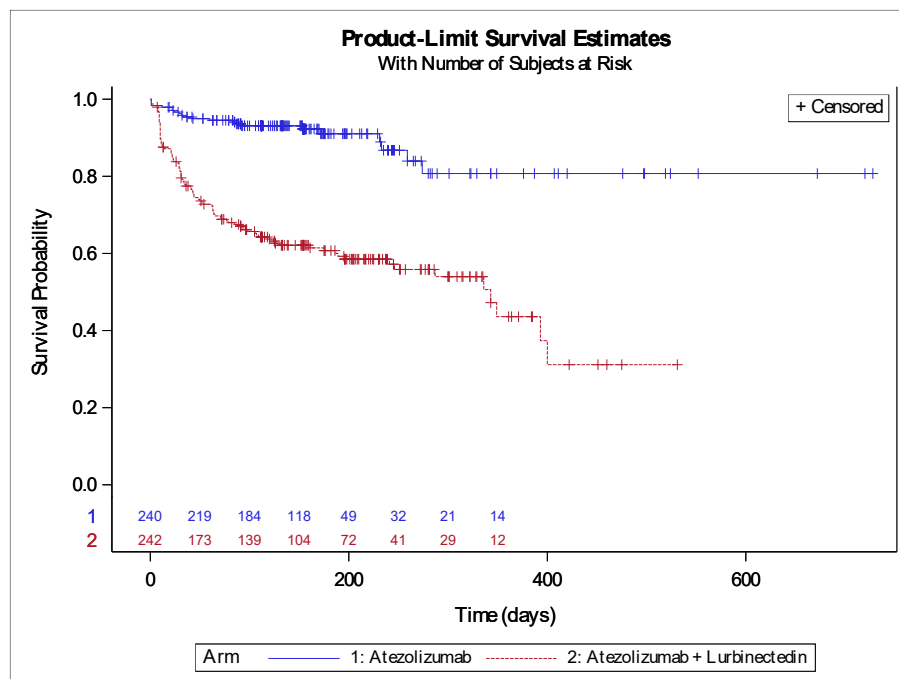


Abbildung 9: Kaplan-Meier plot for any AE (SOC blood and lymphatic system disorders), IMforte trial, Safety Analysis Set, CCOD 29 July 2024

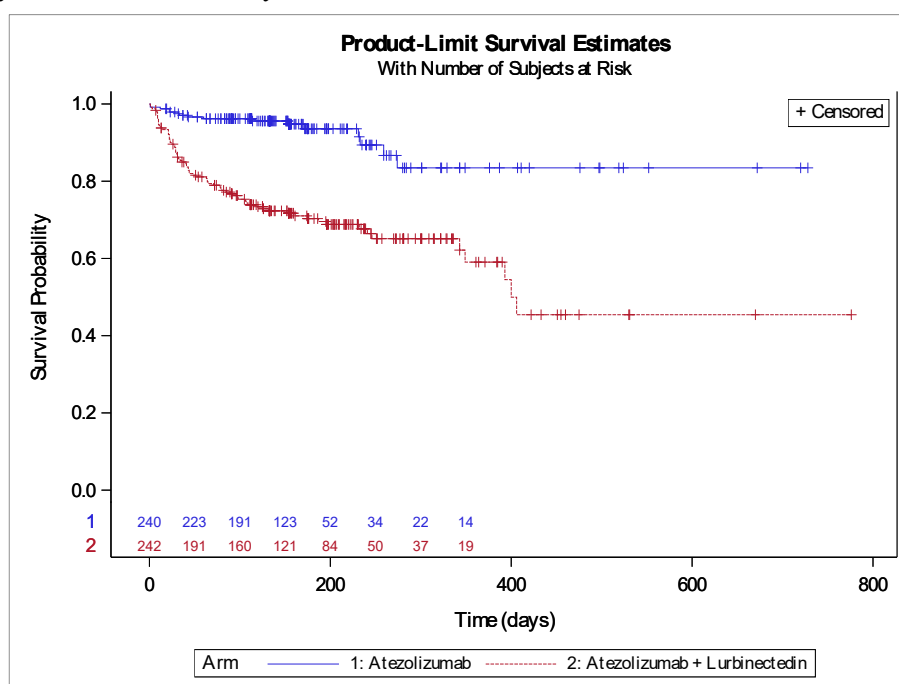


Abbildung 10: Kaplan-Meier plot for any AE (PT anemia), IMforte trial, Safety Analysis Set, CCOD 29 July 2024

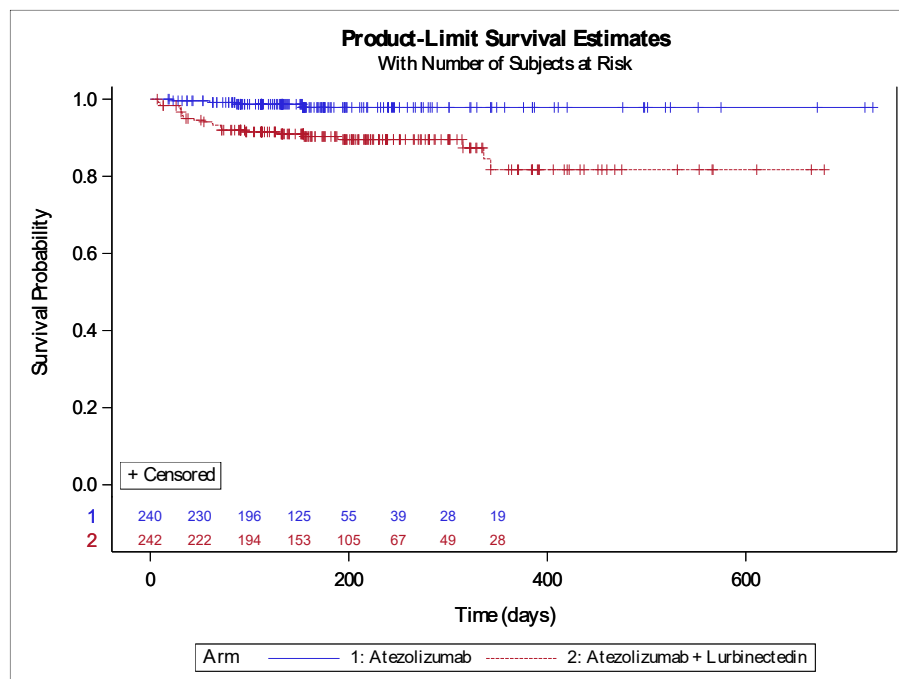


Abbildung 11: Kaplan-Meier plot for any AE (PT neutropenia), IMforte trial, Safety Analysis Set, CCOD 29 July 2024

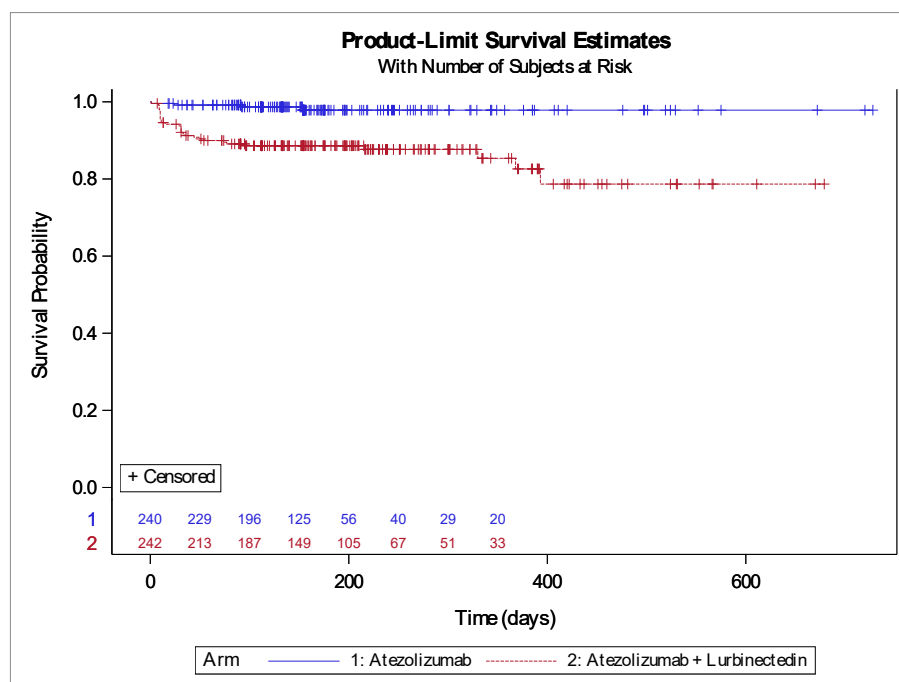


Abbildung 12: Kaplan-Meier plot for any AE (PT thrombocytopenia), IMforte trial, Safety Analysis Set, CCOD 29 July 2024

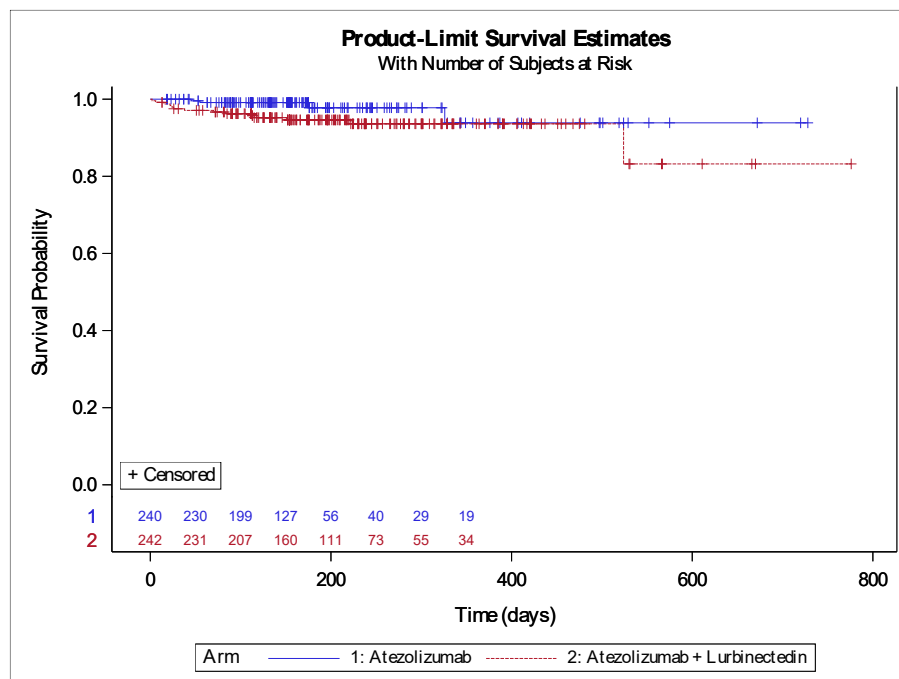


Abbildung 13: Kaplan-Meier plot for any AE (SOC cardiac disorders), IMforte trial, Safety Analysis Set, CCOD 29 July 2024

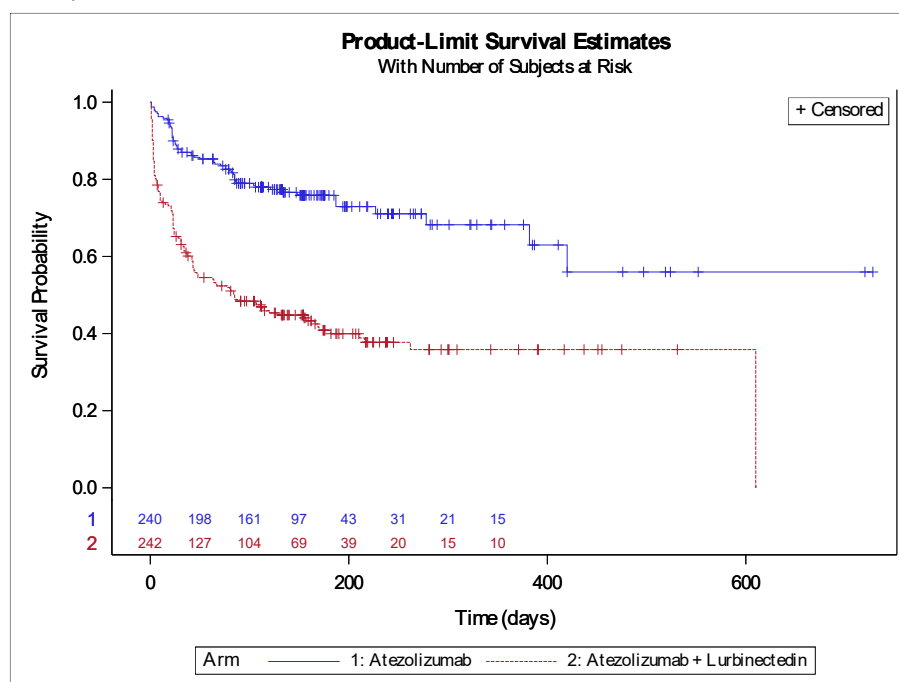


Abbildung 14: Kaplan-Meier plot for any AE (SOC gastrointestinal disorders), IMforte trial, Safety Analysis Set, CCOD 29 July 2024

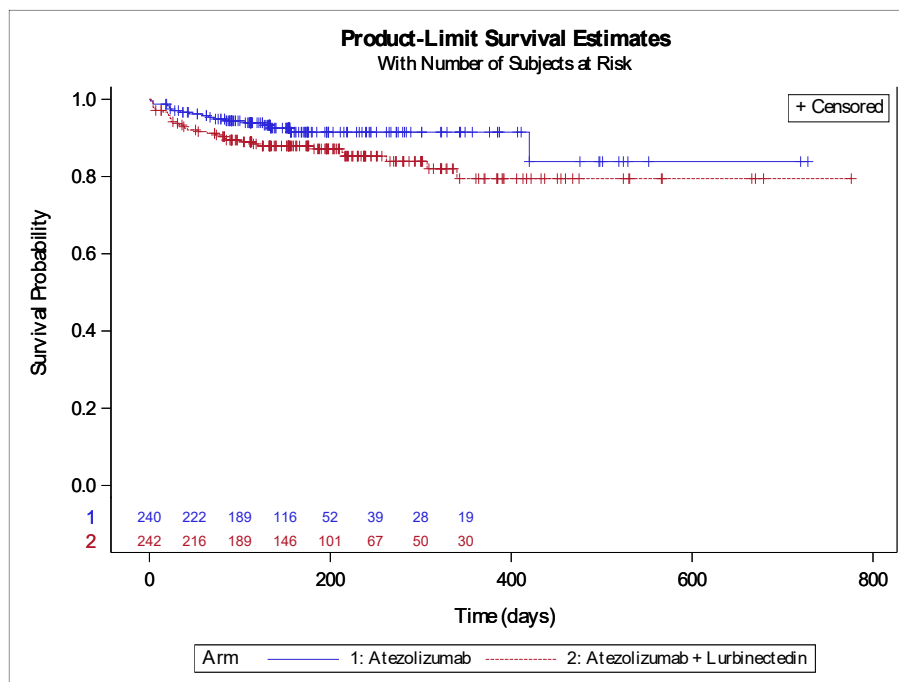


Abbildung 15: Kaplan-Meier plot for any AE (PT diarrhea), IMforte trial, Safety Analysis Set, CCOD 29 July 2024

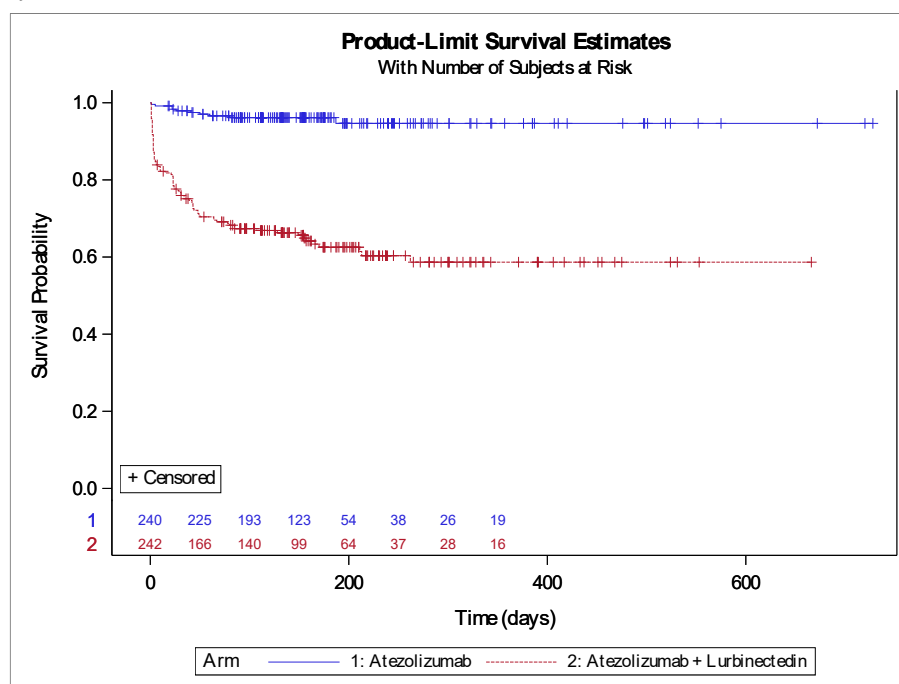


Abbildung 16: Kaplan-Meier plot for any AE (PT nausea), IMforte trial, Safety Analysis Set, CCOD 29 July 2024

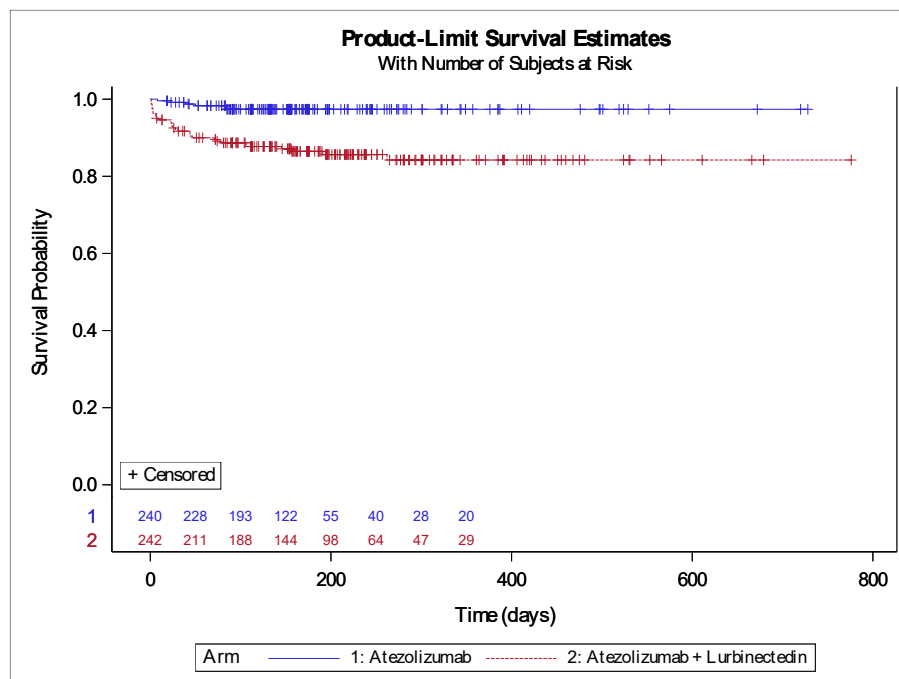


Abbildung 17: Kaplan-Meier plot for any AE (PT vomiting), IMforte trial, Safety Analysis Set, CCOD 29 July 2024

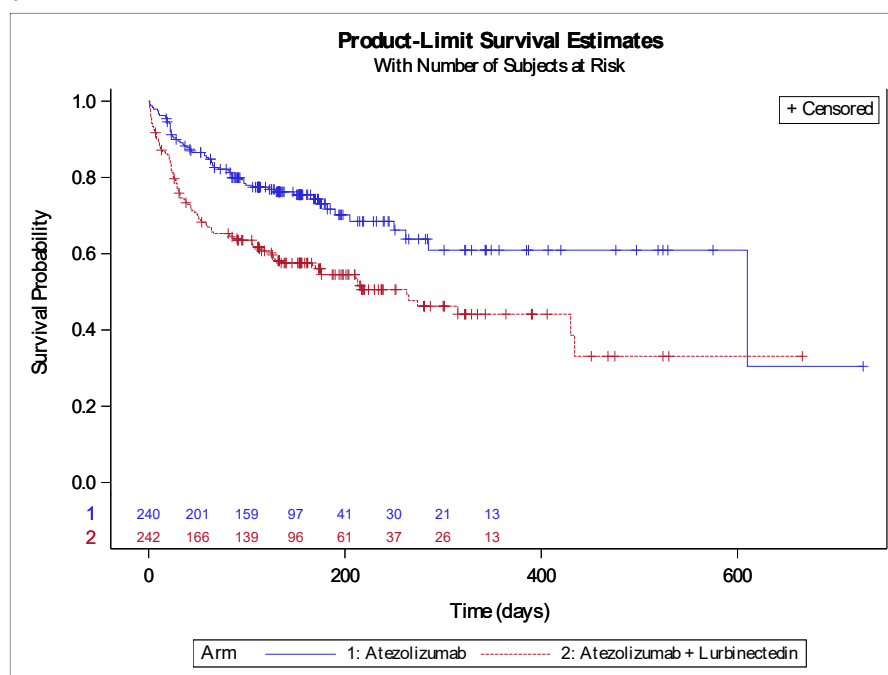


Abbildung 18: Kaplan-Meier plot for any AE (SOC general disorders and administration site conditions), IMforte trial, Safety Analysis Set, CCOD 29 July 2024

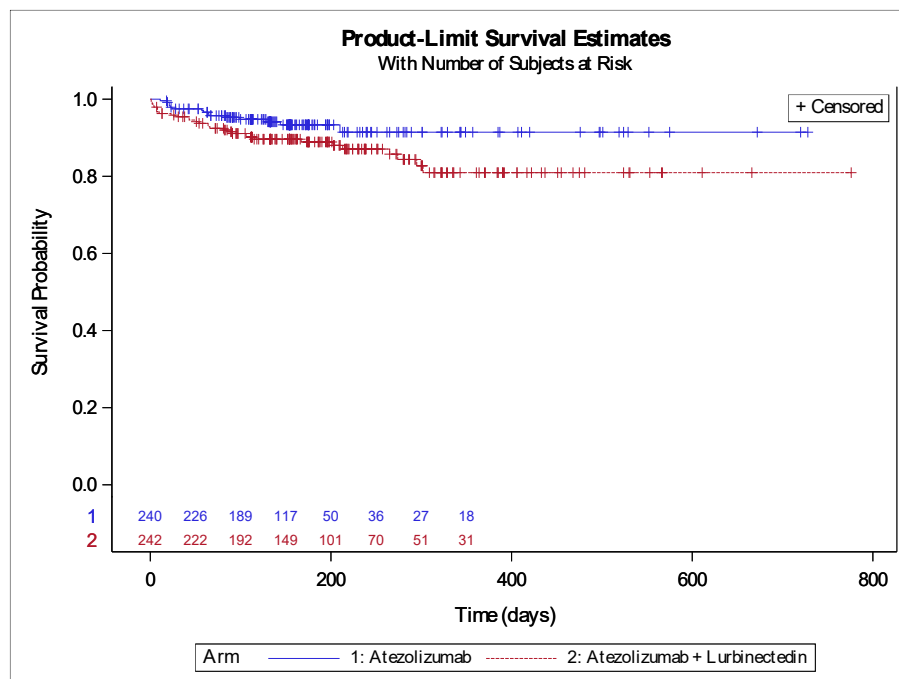


Abbildung 19: Kaplan-Meier plot for any AE (PT asthenia), IMforte trial, Safety Analysis Set, CCOD 29 July 2024

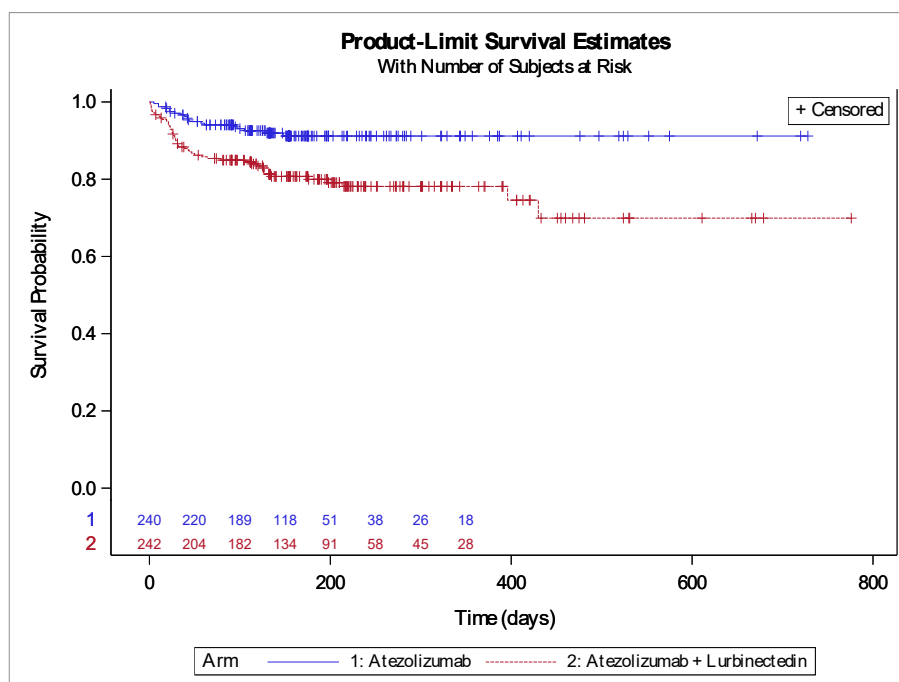


Abbildung 20: Kaplan-Meier plot for any AE (PT fatigue), IMforte trial, Safety Analysis Set, CCOD 29 July 2024

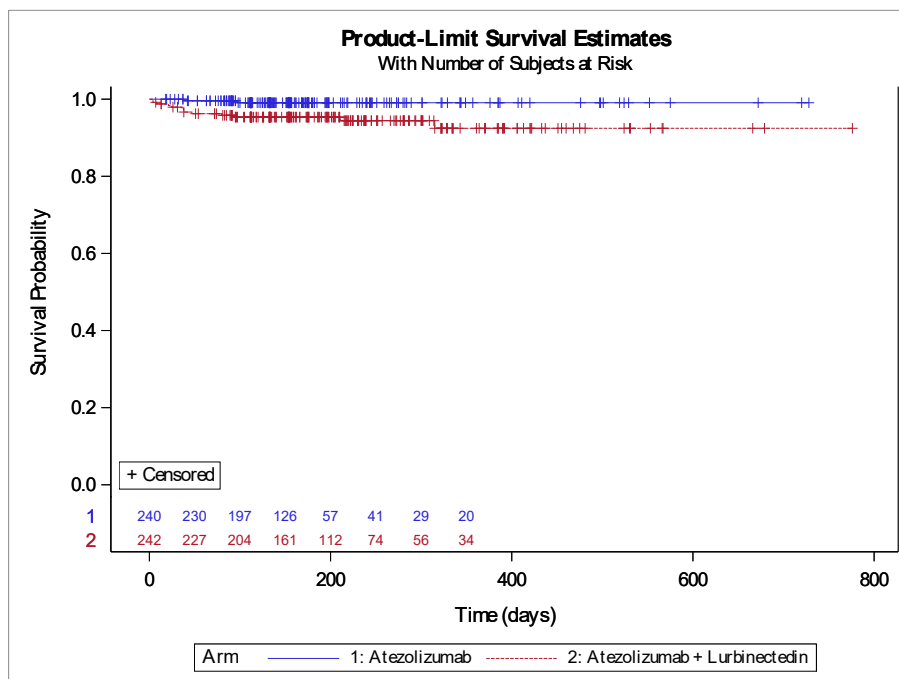


Abbildung 21: Kaplan-Meier plot for any AE (PT pyrexia), IMforte trial, Safety Analysis Set, CCOD 29 July 2024

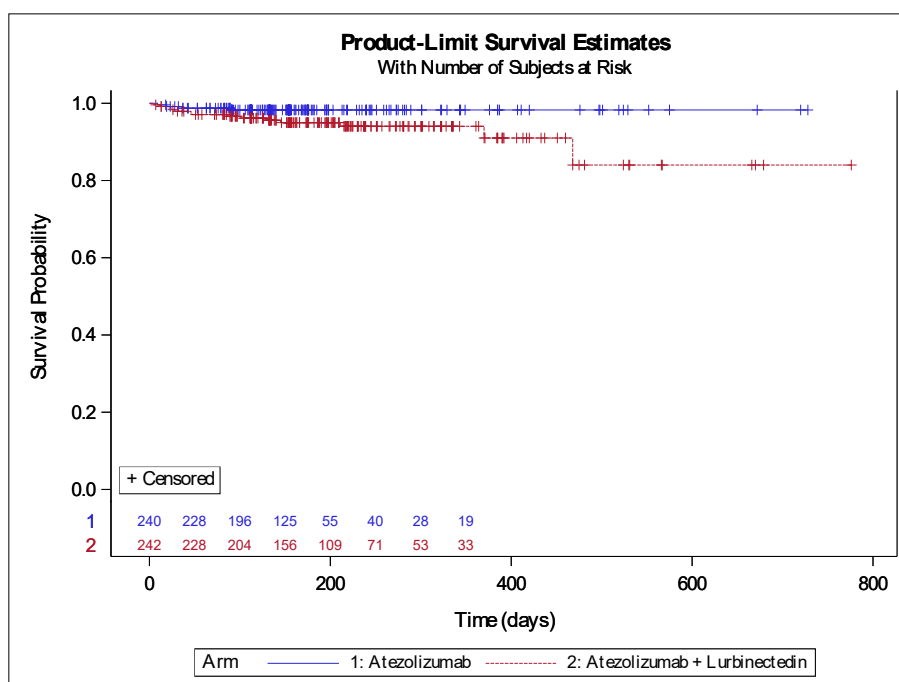


Abbildung 22: Kaplan-Meier plot for any AE (PT COVID-19), IMforte trial, Safety Analysis Set, CCOD 29 July 2024

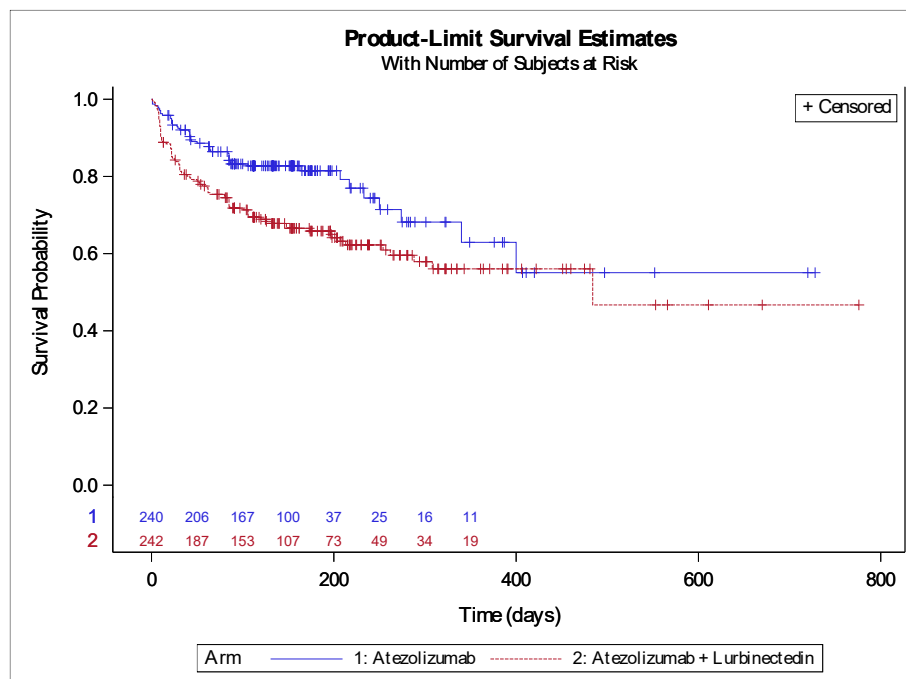


Abbildung 23: Kaplan-Meier plot for any AE (SOC investigations), IMforte trial, Safety Analysis Set, CCOD 29 July 2024

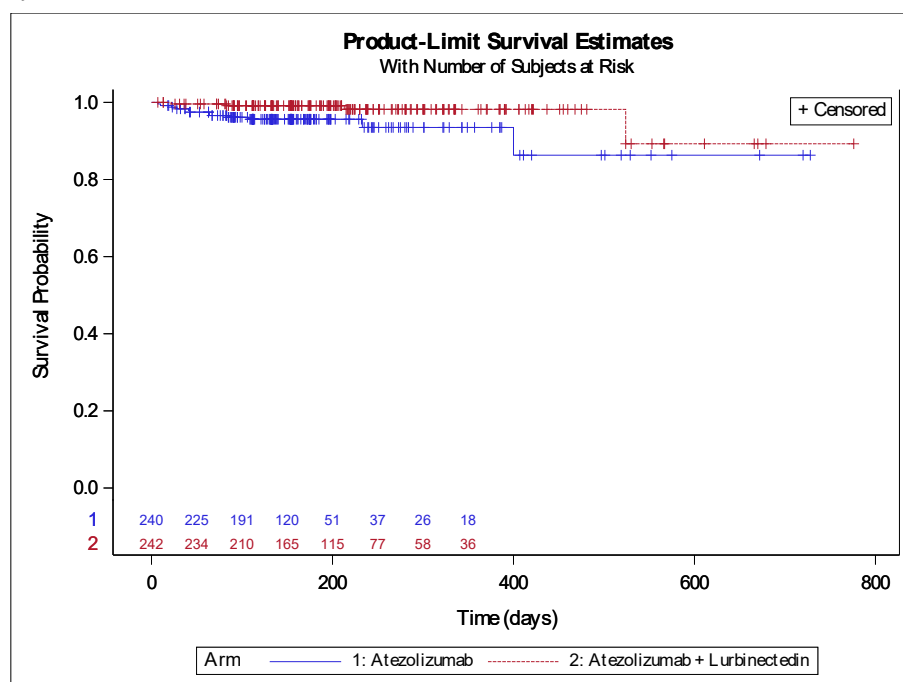


Abbildung 24: Kaplan-Meier plot for any AE (PT blood creatinine phosphokinase increased), IMforte trial, Safety Analysis Set, CCOD 29 July 2024

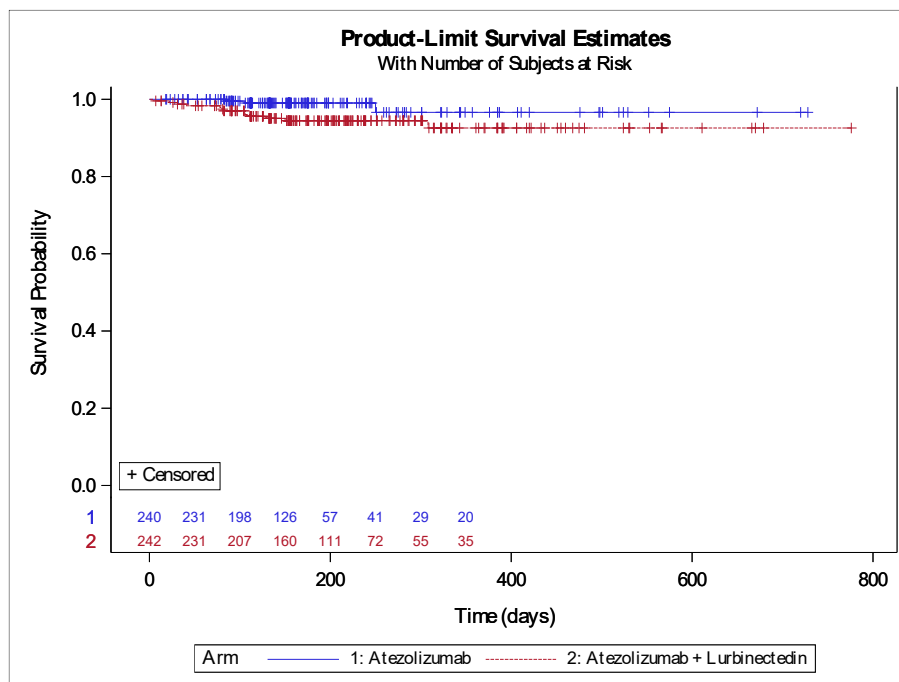


Abbildung 25: Kaplan-Meier plot for any AE (PT blood creatinine increased), IMforte trial, Safety Analysis Set, CCOD 29 July 2024

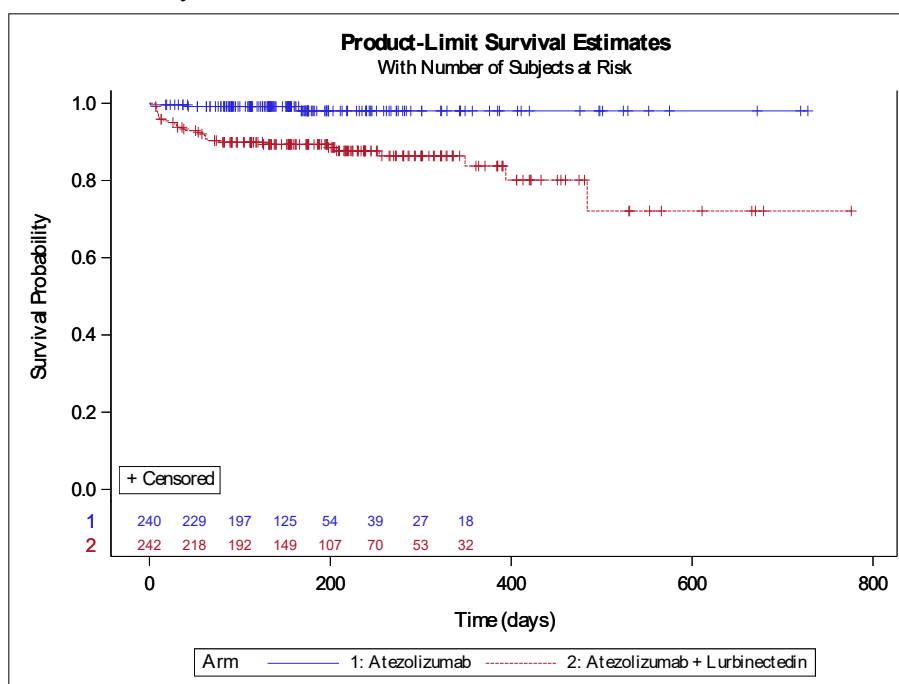


Abbildung 26: Kaplan-Meier plot for any AE (PT neutrophil count decreased), IMforte trial, Safety Analysis Set, CCOD 29 July 2024

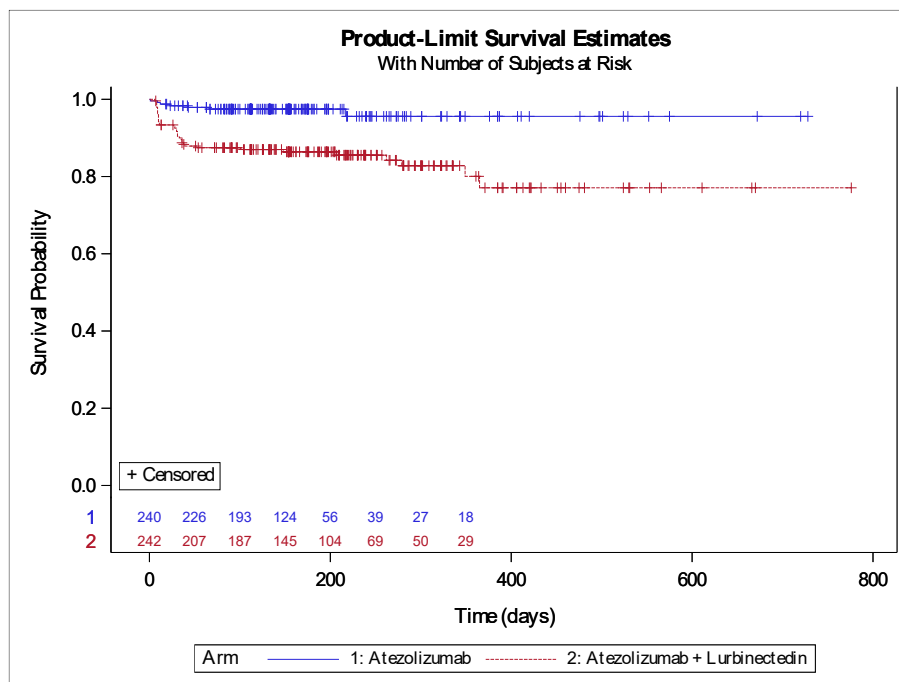


Abbildung 27: Kaplan-Meier plot for any AE (PT platelet count decreased), IMforte trial, Safety Analysis Set, CCOD 29 July 2024

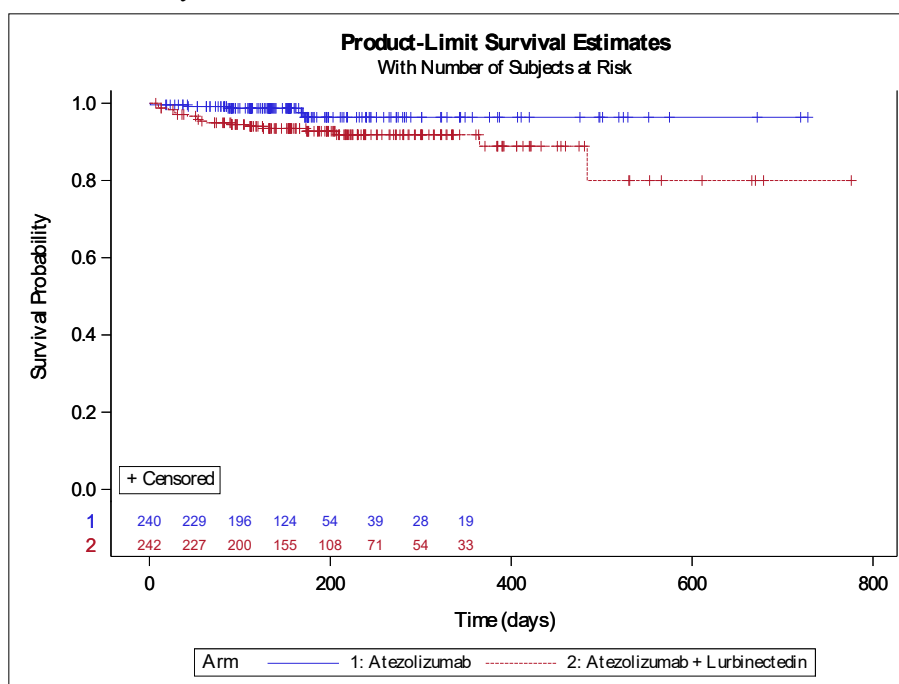


Abbildung 28: Kaplan-Meier plot for any AE (PT white blood cell count decreased), IMforte trial, Safety Analysis Set, CCOD 29 July 2024

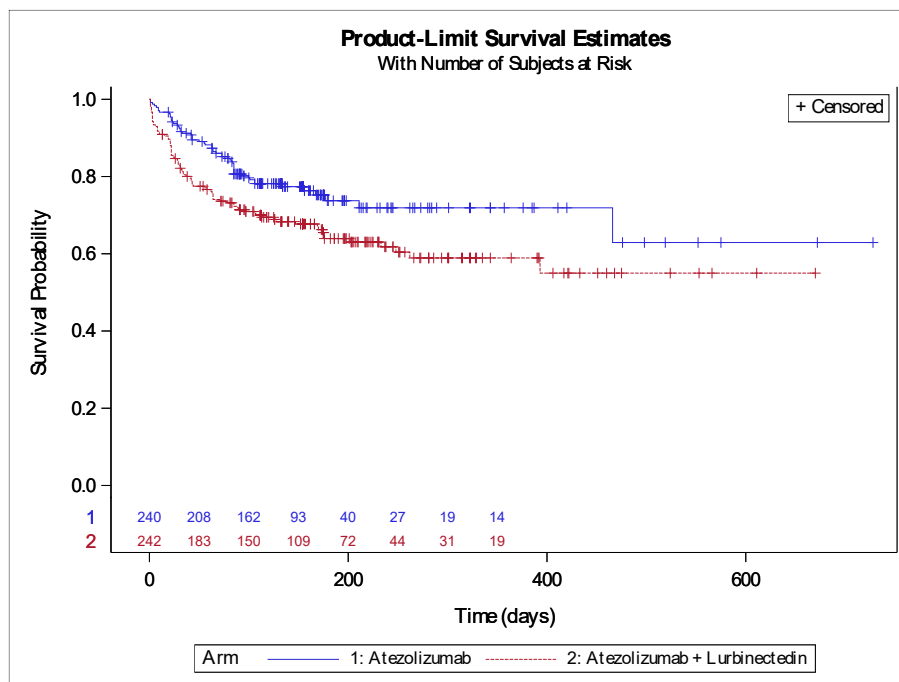


Abbildung 29: Kaplan-Meier plot for any AE (SOC metabolism and nutrition disorders), IMforte trial, Safety Analysis Set, CCOD 29 July 2024

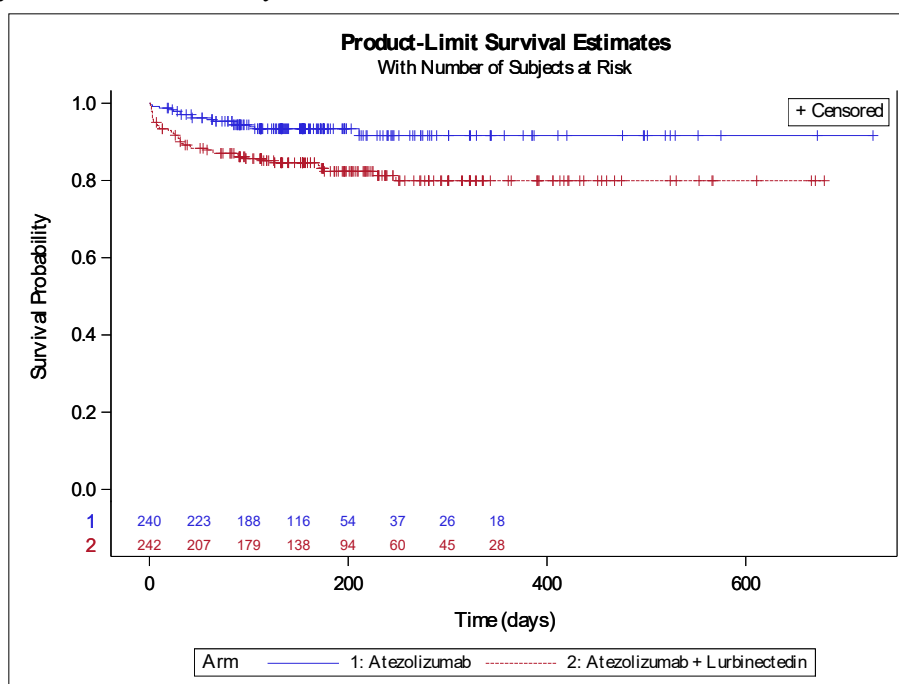


Abbildung 30: Kaplan-Meier plot for any AE (PT decreased appetite), IMforte trial, Safety Analysis Set, CCOD 29 July 2024

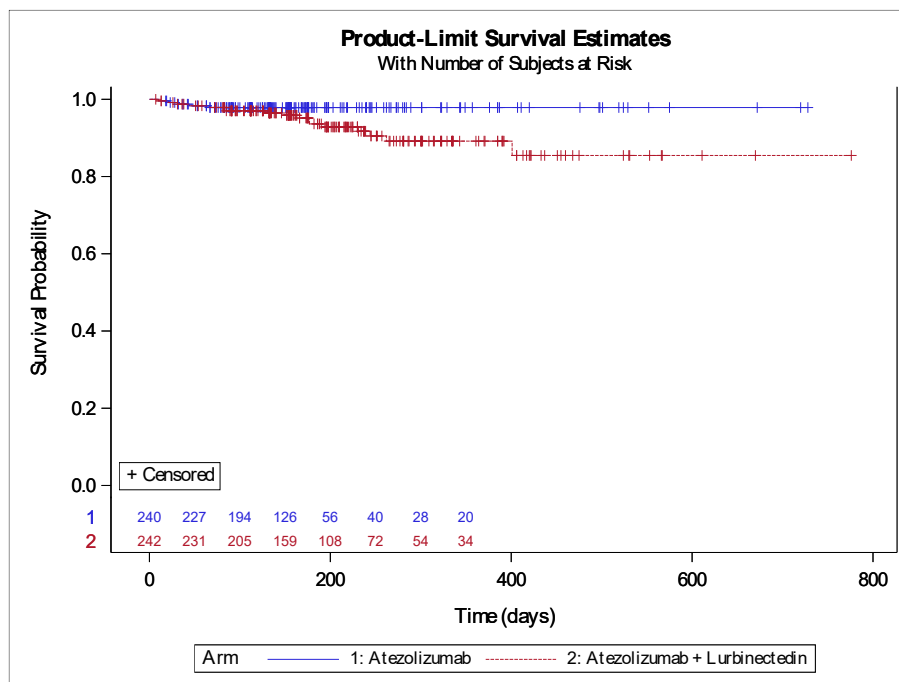


Abbildung 31: Kaplan-Meier plot for any AE (PT dizziness), IMforte trial, Safety Analysis Set, CCOD  
29 July 2024

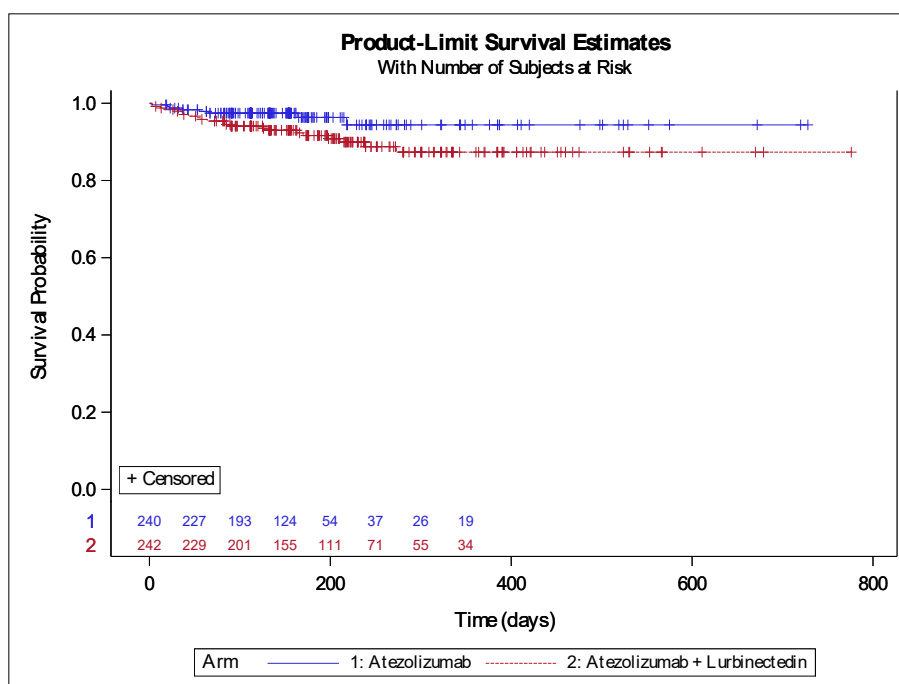


Abbildung 32: Kaplan-Meier plot for any AE (SOC psychiatric disorders), IMforte trial, Safety Analysis Set, CCOD 29 July 2024

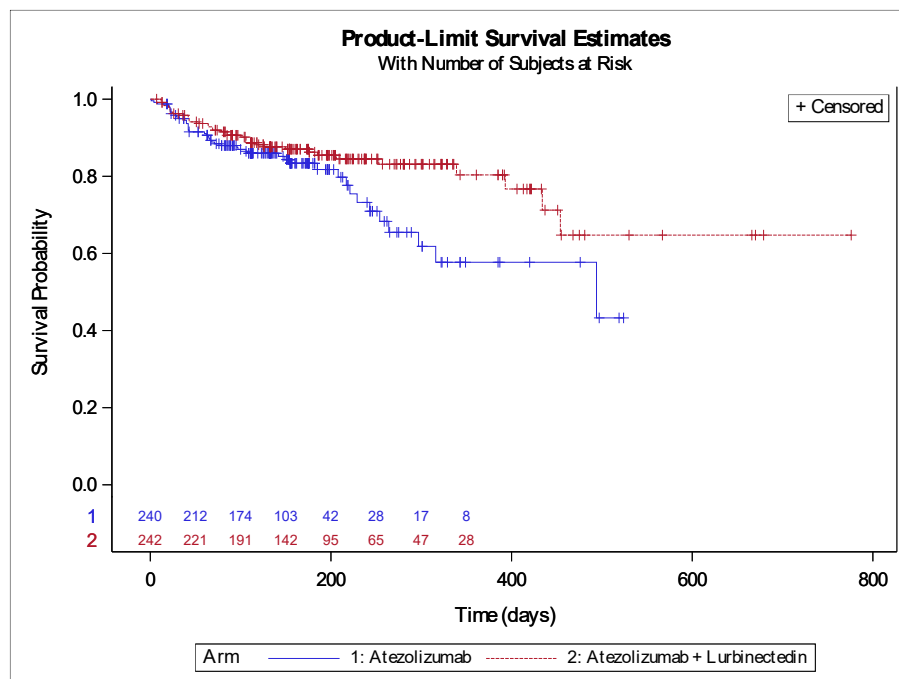


Abbildung 33: Kaplan-Meier plot for any AE (SOC skin and subcutaneous tissue disorders), IMforte trial, Safety Analysis Set, CCOD 29 July 2024

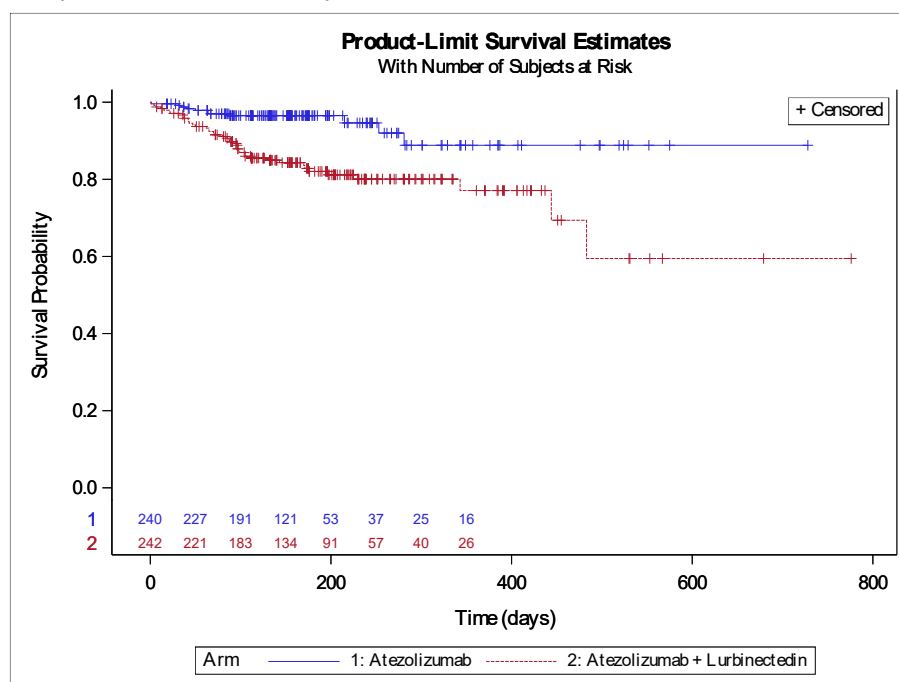


Abbildung 34: Kaplan-Meier plot for any AE (SOC vascular disorders), IMforte trial, Safety Analysis Set, CCOD 29 July 2024

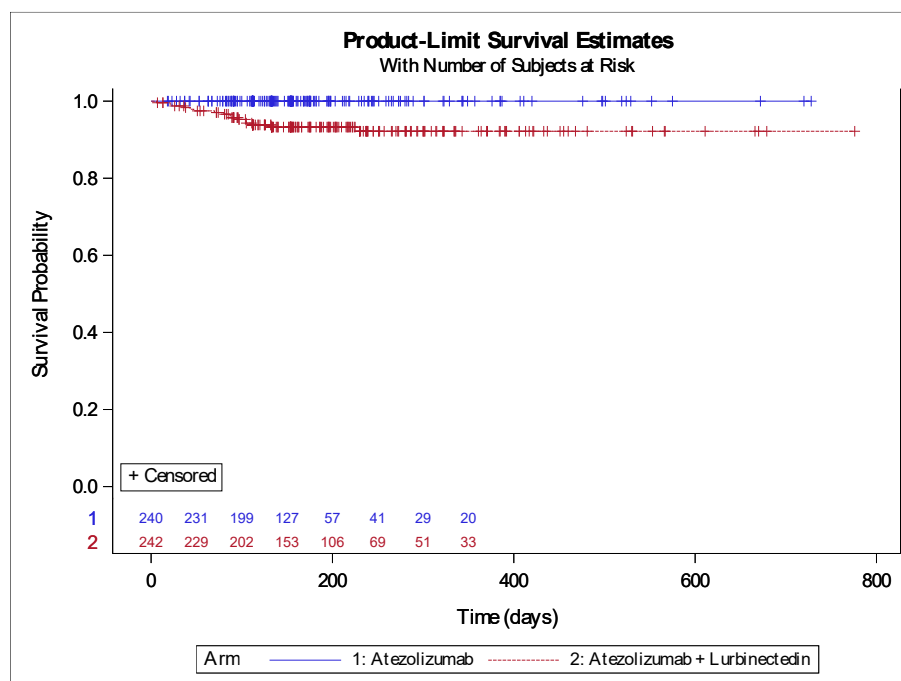


Abbildung 35: Kaplan-Meier plot for any AE (PT phlebitis), IMforte trial, Safety Analysis Set, CCOD  
29 July 2024

Tabelle 4: Severe AE (CTCAE  $\geq 3$ ) by SOC and PT including effect estimates

| Endpoint<br>SOC<br>PT                      | Lurbinectedin + atezolizumab |                                                                                                       | Atezolizumab       |                                                                                                    | Lurbinectedin + atezolizumab vs.<br>atezolizumab |
|--------------------------------------------|------------------------------|-------------------------------------------------------------------------------------------------------|--------------------|----------------------------------------------------------------------------------------------------|--------------------------------------------------|
|                                            | N/N <sup>Cen</sup>           | Median time to event in<br>days <sup>a</sup><br>[95% CI] <sup>b</sup><br>patients with event<br>n (%) | N/N <sup>Cen</sup> | Median time to event in days <sup>a</sup><br>[95% CI] <sup>b</sup><br>patients with event<br>n (%) | HR [95% CI] <sup>c</sup><br>p-value <sup>d</sup> |
| Blood and<br>lymphatic system<br>disorders | 242/203                      | NE [NE; NE]<br>39 (16.1)                                                                              | 240/236            | NE [NE; NE]<br>4 (1.7)                                                                             | 9.35 [3.33; 26.32]<br><.0001                     |
| Anemia                                     | 242/222                      | NE [NE; NE]<br>20 (8.3)                                                                               | 240/238            | NE [NE; NE]<br>2 (0.8)                                                                             | 9.26 [2.16; 40.00]<br>0.0003                     |
| Febrile<br>neutropenia                     | 242/238                      | NE [NE; NE]<br>4 (1.7)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [NE; NE]<br>0.0502                            |
| Leukocytosis                               | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [NE; NE]<br>0.3237                            |
| Leukopenia                                 | 242/240                      | NE [NE; NE]<br>2 (0.8)                                                                                | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                             | 1.81 [0.16; 20.00]<br>0.6232                     |
| Lymphadenitis                              | 242/242                      | NE [NE; NE]<br>0 (0.0)                                                                                | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                             | NE [NE; NE]<br>0.3153                            |
| Lymphopenia                                | 242/239                      | NE [NE; NE]<br>3 (1.2)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [NE; NE]<br>0.1192                            |
| Neutropenia                                | 242/231                      | NE [NE; NE]<br>11 (4.5)                                                                               | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                             | 10.10 [1.30; 76.92]<br>0.0064                    |
| Pancytopenia                               | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [NE; NE]<br>0.4268                            |

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

| Endpoint<br>SOC<br>PT          | Lurbinectedin + atezolizumab |                                                                                                       | Atezolizumab       |                                                                                                    | Lurbinectedin + atezolizumab vs.<br>atezolizumab |
|--------------------------------|------------------------------|-------------------------------------------------------------------------------------------------------|--------------------|----------------------------------------------------------------------------------------------------|--------------------------------------------------|
|                                | N/N <sup>Cen</sup>           | Median time to event in<br>days <sup>a</sup><br>[95% CI] <sup>b</sup><br>patients with event<br>n (%) | N/N <sup>Cen</sup> | Median time to event in days <sup>a</sup><br>[95% CI] <sup>b</sup><br>patients with event<br>n (%) | HR [95% CI] <sup>c</sup><br>p-value <sup>d</sup> |
| Thrombocytopeni<br>a           | 242/231                      | NE [NE; NE]<br>11 (4.5)                                                                               | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                             | 10 [1.29; 76.92]<br>0.0066                       |
| Cardiac disorders              | 242/234                      | NE [NE; NE]<br>8 (3.3)                                                                                | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                             | 6.67 [0.83; 52.63]<br>0.0394                     |
| Acute myocardial<br>infarction | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [NE; NE]<br>0.3554                            |
| Atrial fibrillation            | 242/240                      | NE [NE; NE]<br>2 (0.8)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [NE; NE]<br>0.1569                            |
| Cardio-<br>respiratory arrest  | 242/240                      | NE [NE; NE]<br>2 (0.8)                                                                                | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                             | 1.64 [0.15; 18.52]<br>0.6863                     |
| Myocardial<br>infarction       | 242/239                      | NE [NE; NE]<br>3 (1.2)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [NE; NE]<br>0.1460                            |
| Ear and labyrinth<br>disorders | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [NE; NE]<br>0.3215                            |
| Vertigo                        | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [NE; NE]<br>0.3215                            |
| Endocrine disorders            | 242/242                      | NE [NE; NE]<br>0 (0.0)                                                                                | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                             | NE [NE; NE]<br>0.3131                            |

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

| Endpoint<br>SOC<br>PT          | Lurbinectedin + atezolizumab |                                                                                                       | Atezolizumab       |                                                                                                    | Lurbinectedin + atezolizumab vs.<br>atezolizumab |
|--------------------------------|------------------------------|-------------------------------------------------------------------------------------------------------|--------------------|----------------------------------------------------------------------------------------------------|--------------------------------------------------|
|                                | N/N <sup>Cen</sup>           | Median time to event in<br>days <sup>a</sup><br>[95% CI] <sup>b</sup><br>patients with event<br>n (%) | N/N <sup>Cen</sup> | Median time to event in days <sup>a</sup><br>[95% CI] <sup>b</sup><br>patients with event<br>n (%) | HR [95% CI] <sup>c</sup><br>p-value <sup>d</sup> |
| Adrenal<br>insufficiency       | 242/242                      | NE [NE; NE]<br>0 (0.0)                                                                                | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                             | NE [NE; NE]<br>0.3131                            |
| Gastrointestinal<br>disorders  | 242/233                      | NE [NE; NE]<br>9 (3.7)                                                                                | 240/232            | NE [NE; NE]<br>8 (3.3)                                                                             | 1.05 [0.41; 2.73]<br>0.9176                      |
| Abdominal pain                 | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [NE; NE]<br>0.4332                            |
| Chronic gastritis              | 242/242                      | NE [NE; NE]<br>0 (0.0)                                                                                | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                             | NE [NE; NE]<br>0.2130                            |
| Constipation                   | 242/242                      | NE [NE; NE]<br>0 (0.0)                                                                                | 240/238            | NE [NE; NE]<br>2 (0.8)                                                                             | NE [NE; NE]<br>0.1527                            |
| Diarrhea                       | 242/242                      | NE [NE; NE]<br>0 (0.0)                                                                                | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                             | NE [NE; NE]<br>0.3153                            |
| Gastrointestinal<br>hemorrhage | 242/242                      | NE [NE; NE]<br>0 (0.0)                                                                                | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                             | NE [NE; NE]<br>0.3110                            |
| Ileus                          | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [NE; NE]<br>0.3193                            |
| Nausea                         | 242/236                      | NE [NE; NE]<br>6 (2.5)                                                                                | 240/238            | NE [NE; NE]<br>2 (0.8)                                                                             | 2.99 [0.60; 14.71]<br>0.1592                     |

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

| Endpoint<br>SOC<br>PT                                      | Lurbinectedin + atezolizumab |                                                                                                       | Atezolizumab       |                                                                                                    | Lurbinectedin + atezolizumab vs.<br>atezolizumab |
|------------------------------------------------------------|------------------------------|-------------------------------------------------------------------------------------------------------|--------------------|----------------------------------------------------------------------------------------------------|--------------------------------------------------|
|                                                            | N/N <sup>Cen</sup>           | Median time to event in<br>days <sup>a</sup><br>[95% CI] <sup>b</sup><br>patients with event<br>n (%) | N/N <sup>Cen</sup> | Median time to event in days <sup>a</sup><br>[95% CI] <sup>b</sup><br>patients with event<br>n (%) | HR [95% CI] <sup>c</sup><br>p-value <sup>d</sup> |
| Pancreatitis acute                                         | 242/242                      | NE [NE; NE]<br>0 (0.0)                                                                                | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                             | NE [NE; NE]<br>0.3152                            |
| Pancreatitis<br>chronic                                    | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [NE; NE]<br>0.3327                            |
| Volvulus                                                   | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                             | 0.75 [0.05; 12.35]<br>0.8410                     |
| Vomiting                                                   | 242/240                      | NE [NE; NE]<br>2 (0.8)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [NE; NE]<br>0.1609                            |
| General disorders<br>and administration<br>site conditions | 242/227                      | NE [NE; NE]<br>15 (6.2)                                                                               | 240/231            | NE [NE; NE]<br>9 (3.8)                                                                             | 1.37 [0.60; 3.17]<br>0.4532                      |
| Adhesion                                                   | 242/242                      | NE [NE; NE]<br>0 (0.0)                                                                                | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                             | NE [NE; NE]<br>0.1654                            |
| Asthenia                                                   | 242/239                      | NE [NE; NE]<br>3 (1.2)                                                                                | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                             | 2.27 [0.23; 22.22]<br>0.4686                     |
| Chest pain                                                 | 242/242                      | NE [NE; NE]<br>0 (0.0)                                                                                | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                             | NE [NE; NE]<br>0.1473                            |
| Death                                                      | 242/242                      | NE [NE; NE]<br>0 (0.0)                                                                                | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                             | NE [NE; NE]<br>0.1902                            |

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

| Endpoint<br>SOC<br>PT                       | Lurbinectedin + atezolizumab |                                                                                                       | Atezolizumab       |                                                                                                    | Lurbinectedin + atezolizumab vs.<br>atezolizumab |
|---------------------------------------------|------------------------------|-------------------------------------------------------------------------------------------------------|--------------------|----------------------------------------------------------------------------------------------------|--------------------------------------------------|
|                                             | N/N <sup>Cen</sup>           | Median time to event in<br>days <sup>a</sup><br>[95% CI] <sup>b</sup><br>patients with event<br>n (%) | N/N <sup>Cen</sup> | Median time to event in days <sup>a</sup><br>[95% CI] <sup>b</sup><br>patients with event<br>n (%) | HR [95% CI] <sup>c</sup><br>p-value <sup>d</sup> |
| Fatigue                                     | 242/234                      | NE [NE; NE]<br>8 (3.3)                                                                                | 240/237            | NE [NE; NE]<br>3 (1.3)                                                                             | 2.55 [0.68; 9.62]<br>0.1518                      |
| Gait disturbance                            | 242/242                      | NE [NE; NE]<br>0 (0.0)                                                                                | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                             | NE [NE; NE]<br>0.1573                            |
| General physical<br>health<br>deterioration | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [NE; NE]<br>0.3204                            |
| Influenza like<br>illness                   | 242/242                      | NE [NE; NE]<br>0 (0.0)                                                                                | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                             | NE [NE; NE]<br>0.3153                            |
| Oedema<br>peripheral                        | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [NE; NE]<br>0.4727                            |
| Pain                                        | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [NE; NE]<br>0.3205                            |
| Peripheral<br>swelling                      | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [NE; NE]<br>0.3205                            |
| Hepatobiliary<br>disorders                  | 242/240                      | NE [NE; NE]<br>2 (0.8)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [NE; NE]<br>0.1623                            |
| Cholecystitis                               | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [NE; NE]<br>0.3237                            |

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

| Endpoint<br>SOC<br>PT             | Lurbinectedin + atezolizumab |                                                                                                       | Atezolizumab       |                                                                                                    | Lurbinectedin + atezolizumab vs.<br>atezolizumab |
|-----------------------------------|------------------------------|-------------------------------------------------------------------------------------------------------|--------------------|----------------------------------------------------------------------------------------------------|--------------------------------------------------|
|                                   | N/N <sup>Cen</sup>           | Median time to event in<br>days <sup>a</sup><br>[95% CI] <sup>b</sup><br>patients with event<br>n (%) | N/N <sup>Cen</sup> | Median time to event in days <sup>a</sup><br>[95% CI] <sup>b</sup><br>patients with event<br>n (%) | HR [95% CI] <sup>c</sup><br>p-value <sup>d</sup> |
| Immune-mediated hepatitis         | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [NE; NE]<br>0.3237                            |
| Infections and infestations       | 242/220                      | NE [NE; NE]<br>22 (9.1)                                                                               | 240/224            | NE [NE; NE]<br>16 (6.7)                                                                            | 1.21 [0.63; 2.31]<br>0.5671                      |
| Abscess intestinal                | 242/242                      | NE [NE; NE]<br>0 (0.0)                                                                                | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                             | NE [NE; NE]<br>0.3183                            |
| COVID-19                          | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                             | 0.99 [0.06; 15.87]<br>0.9915                     |
| COVID-19 pneumonia                | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [NE; NE]<br>0.3193                            |
| Cellulitis                        | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [NE; NE]<br>0.3204                            |
| Encephalitis                      | 242/242                      | NE [NE; NE]<br>0 (0.0)                                                                                | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                             | NE [NE; NE]<br>0.2816                            |
| Infection                         | 242/239                      | NE [NE; NE]<br>3 (1.2)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [NE; NE]<br>0.0839                            |
| Lower respiratory tract infection | 242/240                      | NE [NE; NE]<br>2 (0.8)                                                                                | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                             | 1.96 [0.18; 21.74]<br>0.5747                     |

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

| Endpoint<br>SOC<br>PT                  | Lurbinectedin + atezolizumab |                                                                                                       | Atezolizumab       |                                                                                                    | Lurbinectedin + atezolizumab vs.<br>atezolizumab |
|----------------------------------------|------------------------------|-------------------------------------------------------------------------------------------------------|--------------------|----------------------------------------------------------------------------------------------------|--------------------------------------------------|
|                                        | N/N <sup>Cen</sup>           | Median time to event in<br>days <sup>a</sup><br>[95% CI] <sup>b</sup><br>patients with event<br>n (%) | N/N <sup>Cen</sup> | Median time to event in days <sup>a</sup><br>[95% CI] <sup>b</sup><br>patients with event<br>n (%) | HR [95% CI] <sup>c</sup><br>p-value <sup>d</sup> |
| Pharyngitis                            | 242/242                      | NE [NE; NE]<br>0 (0.0)                                                                                | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                             | NE [NE; NE]<br>0.2820                            |
| Pneumocystis<br>jirovecii<br>pneumonia | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [NE; NE]<br>0.3183                            |
| Pneumonia                              | 242/236                      | NE [NE; NE]<br>6 (2.5)                                                                                | 240/234            | NE [NE; NE]<br>6 (2.5)                                                                             | 0.86 [0.27; 2.68]<br>0.7894                      |
| Pneumonia viral                        | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [NE; NE]<br>0.3193                            |
| Pyelonephritis<br>acute                | 242/242                      | NE [NE; NE]<br>0 (0.0)                                                                                | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                             | NE [NE; NE]<br>0.3152                            |
| Respiratory tract<br>infection         | 242/238                      | NE [NE; NE]<br>4 (1.7)                                                                                | 240/238            | NE [NE; NE]<br>2 (0.8)                                                                             | 1.53 [0.28; 8.48]<br>0.6224                      |
| Sepsis                                 | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                             | 0.73 [0.04; 11.91]<br>0.8218                     |
| Septic shock                           | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [NE; NE]<br>0.3194                            |
| Urinary tract<br>infection             | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                             | 0.87 [0.05; 13.89]<br>0.9187                     |

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

| Endpoint<br>SOC<br>PT                                | Lurbinectedin + atezolizumab |                                                                                                       | Atezolizumab       |                                                                                                    | Lurbinectedin + atezolizumab vs.<br>atezolizumab |
|------------------------------------------------------|------------------------------|-------------------------------------------------------------------------------------------------------|--------------------|----------------------------------------------------------------------------------------------------|--------------------------------------------------|
|                                                      | N/N <sup>Cen</sup>           | Median time to event in<br>days <sup>a</sup><br>[95% CI] <sup>b</sup><br>patients with event<br>n (%) | N/N <sup>Cen</sup> | Median time to event in days <sup>a</sup><br>[95% CI] <sup>b</sup><br>patients with event<br>n (%) | HR [95% CI] <sup>c</sup><br>p-value <sup>d</sup> |
| Urosepsis                                            | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [NE; NE]<br>0.3237                            |
| Vascular device<br>infection                         | 242/240                      | NE [NE; NE]<br>2 (0.8)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [NE; NE]<br>0.2238                            |
| Injury, poisoning<br>and procedural<br>complications | 242/240                      | NE [NE; NE]<br>2 (0.8)                                                                                | 240/238            | NE [NE; NE]<br>2 (0.8)                                                                             | 0.69 [0.10; 5.05]<br>0.7157                      |
| Ankle fracture                                       | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [NE; NE]<br>0.4778                            |
| Fall                                                 | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [NE; NE]<br>0.4736                            |
| Femur fracture                                       | 242/242                      | NE [NE; NE]<br>0 (0.0)                                                                                | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                             | NE [NE; NE]<br>0.3153                            |
| Road traffic<br>accident                             | 242/242                      | NE [NE; NE]<br>0 (0.0)                                                                                | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                             | NE [NE; NE]<br>0.3024                            |
| Investigations                                       | 242/212                      | NE [NE; NE]<br>30 (12.4)                                                                              | 240/231            | NE [NE; NE]<br>9 (3.8)                                                                             | 3.21 [1.52; 6.76]<br>0.0013                      |
| Alanine<br>aminotransferase<br>increased             | 242/236                      | NE [NE; NE]<br>6 (2.5)                                                                                | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                             | 5.65 [0.68; 7.62]<br>0.0711                      |

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

| Endpoint<br>SOC<br>PT                                        | Lurbinectedin + atezolizumab |                                                                                                       | Atezolizumab       |                                                                                                    | Lurbinectedin + atezolizumab vs.<br>atezolizumab |
|--------------------------------------------------------------|------------------------------|-------------------------------------------------------------------------------------------------------|--------------------|----------------------------------------------------------------------------------------------------|--------------------------------------------------|
|                                                              | N/N <sup>Cen</sup>           | Median time to event in<br>days <sup>a</sup><br>[95% CI] <sup>b</sup><br>patients with event<br>n (%) | N/N <sup>Cen</sup> | Median time to event in days <sup>a</sup><br>[95% CI] <sup>b</sup><br>patients with event<br>n (%) | HR [95% CI] <sup>c</sup><br>p-value <sup>d</sup> |
| Investigations<br>Aspartate<br>aminotransferase<br>increased | 242/239                      | NE [NE; NE]<br>3 (1.2)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [NE; NE]<br>0.0844                            |
| Blood bilirubin<br>increased                                 | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [NE; NE]<br>0.3258                            |
| Blood creatine<br>phosphokinase<br>increased                 | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                             | 0.97 [0.06; 15.39]<br>0.9812                     |
| Ejection fraction<br>decreased                               | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [NE; NE]<br>0.3183                            |
| Gamma-<br>glutamyltrans-<br>ferase increased                 | 242/240                      | NE [NE; NE]<br>2 (0.8)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [NE; NE]<br>0.1591                            |
| Lipase increased                                             | 242/242                      | NE [NE; NE]<br>0 (0.0)                                                                                | 240/238            | NE [NE; NE]<br>2 (0.8)                                                                             | NE [NE; NE]<br>0.1517                            |
| Liver function<br>test increased                             | 242/242                      | NE [NE; NE]<br>0 (0.0)                                                                                | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                             | NE [NE; NE]<br>0.3163                            |
| Lymphocyte<br>count decreased                                | 242/240                      | NE [NE; NE]<br>2 (0.8)                                                                                | 240/237            | NE [NE; NE]<br>3 (1.3)                                                                             | 0.63 [0.10; 3.76]<br>0.6045                      |
| Neutrophil count<br>decreased                                | 242/224                      | NE [NE; NE]<br>18 (7.4)                                                                               | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [NE; NE]<br><.0001                            |

| Endpoint<br>SOC<br>PT                 | Lurbinectedin + atezolizumab |                                                                                                       | Atezolizumab       |                                                                                                    | Lurbinectedin + atezolizumab vs.<br>atezolizumab |
|---------------------------------------|------------------------------|-------------------------------------------------------------------------------------------------------|--------------------|----------------------------------------------------------------------------------------------------|--------------------------------------------------|
|                                       | N/N <sup>Cen</sup>           | Median time to event in<br>days <sup>a</sup><br>[95% CI] <sup>b</sup><br>patients with event<br>n (%) | N/N <sup>Cen</sup> | Median time to event in days <sup>a</sup><br>[95% CI] <sup>b</sup><br>patients with event<br>n (%) | HR [95% CI] <sup>c</sup><br>p-value <sup>d</sup> |
| Platelet count<br>decreased           | 242/225                      | NE [NE; NE]<br>17 (7.0)                                                                               | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [NE; NE]<br><.0001                            |
| Transaminases<br>increased            | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [NE; NE]<br>0.4268                            |
| Weight increased                      | 242/242                      | NE [NE; NE]<br>0 (0.0)                                                                                | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                             | NE [NE; NE]<br>0.3163                            |
| White blood cell<br>count decreased   | 242/237                      | NE [NE; NE]<br>5 (2.1)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [NE; NE]<br>0.0327                            |
| Metabolism and<br>nutrition disorders | 242/226                      | NE [NE; NE]<br>16 (6.6)                                                                               | 240/228            | NE [NE; NE]<br>12 (5.0)                                                                            | 1.16 [0.55; 2.47]<br>0.6944                      |
| Acidosis                              | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [NE; NE]<br>0.3260                            |
| Alkalosis                             | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [NE; NE]<br>0.3258                            |
| Decreased<br>appetite                 | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [NE; NE]<br>0.3193                            |
| Diabetes mellitus                     | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [NE; NE]<br>0.3194                            |

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

| Endpoint<br>SOC<br>PT    | Lurbinectedin + atezolizumab |                                                                                                       | Atezolizumab       |                                                                                                    | Lurbinectedin + atezolizumab vs.<br>atezolizumab |
|--------------------------|------------------------------|-------------------------------------------------------------------------------------------------------|--------------------|----------------------------------------------------------------------------------------------------|--------------------------------------------------|
|                          | N/N <sup>Cen</sup>           | Median time to event in<br>days <sup>a</sup><br>[95% CI] <sup>b</sup><br>patients with event<br>n (%) | N/N <sup>Cen</sup> | Median time to event in days <sup>a</sup><br>[95% CI] <sup>b</sup><br>patients with event<br>n (%) | HR [95% CI] <sup>c</sup><br>p-value <sup>d</sup> |
| Diabetic<br>ketoacidosis | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [NE; NE]<br>0.3194                            |
| Hyperglycemia            | 242/239                      | NE [NE; NE]<br>3 (1.2)                                                                                | 240/238            | NE [NE; NE]<br>2 (0.8)                                                                             | 1.31 [0.22; 7.94]<br>0.7684                      |
| Hyperkalemia             | 242/242                      | NE [NE; NE]<br>0 (0.0)                                                                                | 240/238            | NE [NE; NE]<br>2 (0.8)                                                                             | NE [NE; NE]<br>0.1522                            |
| Hypertriglyceride<br>mia | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [NE; NE]<br>0.3813                            |
| Hypoalbuminemi<br>a      | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [NE; NE]<br>0.3237                            |
| Hypocalcemia             | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [NE; NE]<br>0.3183                            |
| Hypokalemia              | 242/237                      | NE [NE; NE]<br>5 (2.1)                                                                                | 240/237            | NE [NE; NE]<br>3 (1.3)                                                                             | 1.45 [0.34; 6.14]<br>0.6112                      |
| Hypomagnesemia           | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [NE; NE]<br>0.3183                            |
| Hyponatremia             | 242/239                      | NE [NE; NE]<br>3 (1.2)                                                                                | 240/235            | NE [NE; NE]<br>5 (2.1)                                                                             | 0.47 [0.11; 1.98]<br>0.2907                      |

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

| Endpoint<br>SOC<br>PT                                                        | Lurbinectedin + atezolizumab |                                                                                                       | Atezolizumab       |                                                                                                    | Lurbinectedin + atezolizumab vs.<br>atezolizumab |
|------------------------------------------------------------------------------|------------------------------|-------------------------------------------------------------------------------------------------------|--------------------|----------------------------------------------------------------------------------------------------|--------------------------------------------------|
|                                                                              | N/N <sup>Cen</sup>           | Median time to event in<br>days <sup>a</sup><br>[95% CI] <sup>b</sup><br>patients with event<br>n (%) | N/N <sup>Cen</sup> | Median time to event in days <sup>a</sup><br>[95% CI] <sup>b</sup><br>patients with event<br>n (%) | HR [95% CI] <sup>c</sup><br>p-value <sup>d</sup> |
| Musculoskeletal<br>and connective<br>tissue disorders                        | 242/237                      | NE [NE; NE]<br>5 (2.1)                                                                                | 240/236            | NE [NE; NE]<br>4 (1.7)                                                                             | 1.02 [0.27; 3.86]<br>0.9736                      |
| Arthralgia                                                                   | 242/239                      | NE [NE; NE]<br>3 (1.2)                                                                                | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                             | 2.25 [0.23; 22.22]<br>0.4755                     |
| Back pain                                                                    | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                             | 0.99 [0.06; 15.87]<br>0.9939                     |
| Mobility<br>decreased                                                        | 242/242                      | NE [NE; NE]<br>0 (0.0)                                                                                | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                             | NE [NE; NE]<br>0.3132                            |
| Osteonecrosis of<br>jaw                                                      | 242/242                      | NE [NE; NE]<br>0 (0.0)                                                                                | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                             | NE [NE; NE]<br>0.3142                            |
| Pain in extremity                                                            | 242/241                      | NE [NE; NE]<br>0 (0.0)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [NE; NE]<br>0.4475                            |
| Neoplasms benign,<br>malignant and<br>unspecified (incl<br>cysts and polyps) | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [NE; NE]<br>0.4386                            |
| Acute myeloid<br>leukemia                                                    | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [NE; NE]<br>0.4386                            |
| Nervous system<br>disorders                                                  | 242/236                      | NE [NE; NE]<br>6 (2.5)                                                                                | 240/234            | NE [NE; NE]<br>6 (2.5)                                                                             | 0.76 [0.24; 2.38]<br>0.6331                      |

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

| Endpoint<br>SOC<br>PT               | Lurbinectedin + atezolizumab |                                                                                                       | Atezolizumab       |                                                                                                    | Lurbinectedin + atezolizumab vs.<br>atezolizumab |
|-------------------------------------|------------------------------|-------------------------------------------------------------------------------------------------------|--------------------|----------------------------------------------------------------------------------------------------|--------------------------------------------------|
|                                     | N/N <sup>Cen</sup>           | Median time to event in<br>days <sup>a</sup><br>[95% CI] <sup>b</sup><br>patients with event<br>n (%) | N/N <sup>Cen</sup> | Median time to event in days <sup>a</sup><br>[95% CI] <sup>b</sup><br>patients with event<br>n (%) | HR [95% CI] <sup>c</sup><br>p-value <sup>d</sup> |
| Cerebrovascular<br>accident         | 242/242                      | NE [NE; NE]<br>0 (0.0)                                                                                | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                             | NE [NE; NE]<br>0.3163                            |
| Hypoesthesia                        | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [NE; NE]<br>0.3183                            |
| Neuralgia                           | 242/242                      | NE [NE; NE]<br>0 (0.0)                                                                                | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                             | NE [NE; NE]<br>0.2707                            |
| Neuropathy<br>peripheral            | 242/242                      | NE [NE; NE]<br>0 (0.0)                                                                                | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                             | NE [NE; NE]<br>0.3132                            |
| Peripheral motor<br>neuropathy      | 242/242                      | NE [NE; NE]<br>0 (0.0)                                                                                | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                             | NE [NE; NE]<br>0.1573                            |
| Peripheral<br>sensory<br>neuropathy | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [NE; NE]<br>0.3337                            |
| Sciatica                            | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [NE; NE]<br>0.4268                            |
| Seizure                             | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [NE; NE]<br>0.4679                            |
| Spinal cord<br>compression          | 242/242                      | NE [NE; NE]<br>0 (0.0)                                                                                | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                             | NE [NE; NE]<br>0.3086                            |

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

| Endpoint<br>SOC<br>PT       | Lurbinectedin + atezolizumab |                                                                                                       | Atezolizumab       |                                                                                                    | Lurbinectedin + atezolizumab vs.<br>atezolizumab |
|-----------------------------|------------------------------|-------------------------------------------------------------------------------------------------------|--------------------|----------------------------------------------------------------------------------------------------|--------------------------------------------------|
|                             | N/N <sup>Cen</sup>           | Median time to event in<br>days <sup>a</sup><br>[95% CI] <sup>b</sup><br>patients with event<br>n (%) | N/N <sup>Cen</sup> | Median time to event in days <sup>a</sup><br>[95% CI] <sup>b</sup><br>patients with event<br>n (%) | HR [95% CI] <sup>c</sup><br>p-value <sup>d</sup> |
| Syncope                     | 242/240                      | NE [NE; NE]<br>2 (0.8)                                                                                | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                             | 1.36 [0.12; 15.39]<br>0.8037                     |
| Psychiatric disorders       | 242/240                      | NE [NE; NE]<br>2 (0.8)                                                                                | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                             | 1.07 [0.10; 11.77]<br>0.9586                     |
| Completed suicide           | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [NE; NE]<br>0.4733                            |
| Delirium                    | 242/242                      | NE [NE; NE]<br>0 (0.0)                                                                                | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                             | NE [NE; NE]<br>0.1654                            |
| Depression                  | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [NE; NE]<br>0.4442                            |
| Renal and urinary disorders | 242/236                      | NE [NE; NE]<br>6 (2.5)                                                                                | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                             | 5.46 [0.66; 45.46]<br>0.0777                     |
| Acute kidney injury         | 242/239                      | NE [NE; NE]<br>3 (1.2)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [NE; NE]<br>0.0966                            |
| Immune-mediated nephritis   | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [NE; NE]<br>0.4268                            |
| Nephropathy                 | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [NE; NE]<br>0.3183                            |

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

| Endpoint<br>SOC<br>PT                                    | Lurbinectedin + atezolizumab |                                                                                                       | Atezolizumab       |                                                                                                    | Lurbinectedin + atezolizumab vs.<br>atezolizumab |
|----------------------------------------------------------|------------------------------|-------------------------------------------------------------------------------------------------------|--------------------|----------------------------------------------------------------------------------------------------|--------------------------------------------------|
|                                                          | N/N <sup>Cen</sup>           | Median time to event in<br>days <sup>a</sup><br>[95% CI] <sup>b</sup><br>patients with event<br>n (%) | N/N <sup>Cen</sup> | Median time to event in days <sup>a</sup><br>[95% CI] <sup>b</sup><br>patients with event<br>n (%) | HR [95% CI] <sup>c</sup><br>p-value <sup>d</sup> |
| Perinephric<br>collection                                | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [NE; NE]<br>0.4682                            |
| Renal failure                                            | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [NE; NE]<br>0.3194                            |
| Urinary retention                                        | 242/242                      | NE [NE; NE]<br>0 (0.0)                                                                                | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                             | NE [NE; NE]<br>0.3163                            |
| Respiratory,<br>thoracic and<br>mediastinal<br>disorders | 242/229                      | NE [NE; NE]<br>13 (5.4)                                                                               | 240/235            | NE [NE; NE]<br>5 (2.1)                                                                             | 2.29 [0.81; 6.45]<br>0.1068                      |
| Asthma                                                   | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/240            | NE [NE; NE]<br>(0.0)                                                                               | NE [NE; NE]<br>0.3193                            |
| Bronchospasm                                             | 242/242                      | NE [NE; NE]<br>0 (0.0)                                                                                | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                             | NE [NE; NE]<br>0.3163                            |
| Dyspnea                                                  | 242/237                      | NE [NE; NE]<br>5 (2.1)                                                                                | 240/236            | NE [NE; NE]<br>4 (1.7)                                                                             | 1 [0.27; 3.79]<br>0.9965                         |
| Hemoptysis                                               | 242/240                      | NE [NE; NE]<br>2 (0.8)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [NE; NE]<br>0.2134                            |
| Hypoxia                                                  | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [NE; NE]<br>0.3258                            |

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

| Endpoint<br>SOC<br>PT                  | Lurbinectedin + atezolizumab |                                                                                                       | Atezolizumab       |                                                                                                    | Lurbinectedin + atezolizumab vs.<br>atezolizumab |
|----------------------------------------|------------------------------|-------------------------------------------------------------------------------------------------------|--------------------|----------------------------------------------------------------------------------------------------|--------------------------------------------------|
|                                        | N/N <sup>Cen</sup>           | Median time to event in<br>days <sup>a</sup><br>[95% CI] <sup>b</sup><br>patients with event<br>n (%) | N/N <sup>Cen</sup> | Median time to event in days <sup>a</sup><br>[95% CI] <sup>b</sup><br>patients with event<br>n (%) | HR [95% CI] <sup>c</sup><br>p-value <sup>d</sup> |
| Immune-mediated lung disease           | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [NE; NE]<br>0.3193                            |
| Pleural effusion                       | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [NE; NE]<br>0.3541                            |
| Pneumonitis                            | 242/240                      | NE [NE; NE]<br>2 (0.8)                                                                                | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                             | 1.64 [0.15; 18.52]<br>0.6850                     |
| Productive cough                       | 242/242                      | NE [NE; NE]<br>0 (0.0)                                                                                | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                             | NE [NE; NE]<br>0.1482                            |
| Pulmonary embolism                     | 242/240                      | NE [NE; NE]<br>2 (0.8)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [NE; NE]<br>0.1748                            |
| Respiratory failure                    | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [NE; NE]<br>0.3237                            |
| Skin and subcutaneous tissue disorders | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                             | 0.53 [0.03; 8.40]<br>0.6428                      |
| Pruritus                               | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [NE; NE]<br>0.4475                            |
| Superficial inflammatory dermatosis    | 242/242                      | NE [NE; NE]<br>0 (0.0)                                                                                | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                             | NE [NE; NE]<br>0.1620                            |

| Endpoint<br>SOC<br>PT                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | Lurbinectedin + atezolizumab |                                                                                                       | Atezolizumab       |                                                                                                    | Lurbinectedin + atezolizumab vs.<br>atezolizumab |
|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------|-------------------------------------------------------------------------------------------------------|--------------------|----------------------------------------------------------------------------------------------------|--------------------------------------------------|
|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          | N/N <sup>Cen</sup>           | Median time to event in<br>days <sup>a</sup><br>[95% CI] <sup>b</sup><br>patients with event<br>n (%) | N/N <sup>Cen</sup> | Median time to event in days <sup>a</sup><br>[95% CI] <sup>b</sup><br>patients with event<br>n (%) | HR [95% CI] <sup>c</sup><br>p-value <sup>d</sup> |
| Vascular disorders                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       | 242/239                      | NE [NE; NE]<br>3 (1.2)                                                                                | 240/238            | NE [NE; NE]<br>2 (0.8)                                                                             | 1.35 [0.22; 8.13]<br>0.7425                      |
| Arteriosclerosis                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [NE; NE]<br>0.4268                            |
| Hypertension                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             | 242/242                      | NE [NE; NE]<br>0 (0.0)                                                                                | 240/238            | NE [NE; NE]<br>2 (0.8)                                                                             | NE [NE; NE]<br>0.1524                            |
| Thrombophlebitis                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [NE; NE]<br>0.3314                            |
| Thrombosis                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [NE; NE]<br>0.3194                            |
| <p>CCOD: 29 July 2024; NE: not estimable.<br/>           If a patient experienced either repeated occurrences of the same adverse event or two different adverse events, one Grade 3 and one Grade 4, they are counted only once in the Grade <math>\geq 3</math> category.<br/>           a: summaries of duration (median) are Kaplan-Meier estimates.<br/>           b: 95% CIs for the median were computed using the method of Brookmeyer and Crowley.<br/>           c: hazard ratios were estimated using a stratified Cox proportional hazard model. The stratification factors are ECOG PS at randomization (0 vs. 1), LDH at randomization (<math>\leq</math>ULN vs <math>&gt;</math>ULN) via local laboratory test, presence of liver metastases at enrollment (yes vs. no), and prior receipt of PCI (yes vs. no).<br/>           d: p-value based on the log rank test.</p> |                              |                                                                                                       |                    |                                                                                                    |                                                  |

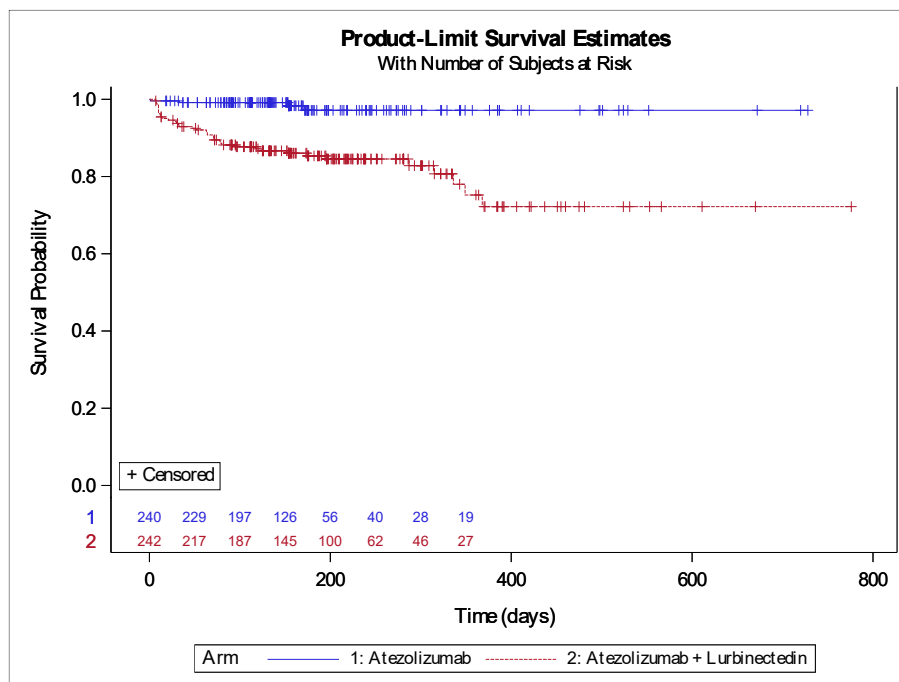


Abbildung 36: Kaplan-Meier plot for grade  $\geq 3$  AE (SOC blood and lymphatic system disorders), IMforte trial, Safety Analysis Set, CCOD 29 July 2024

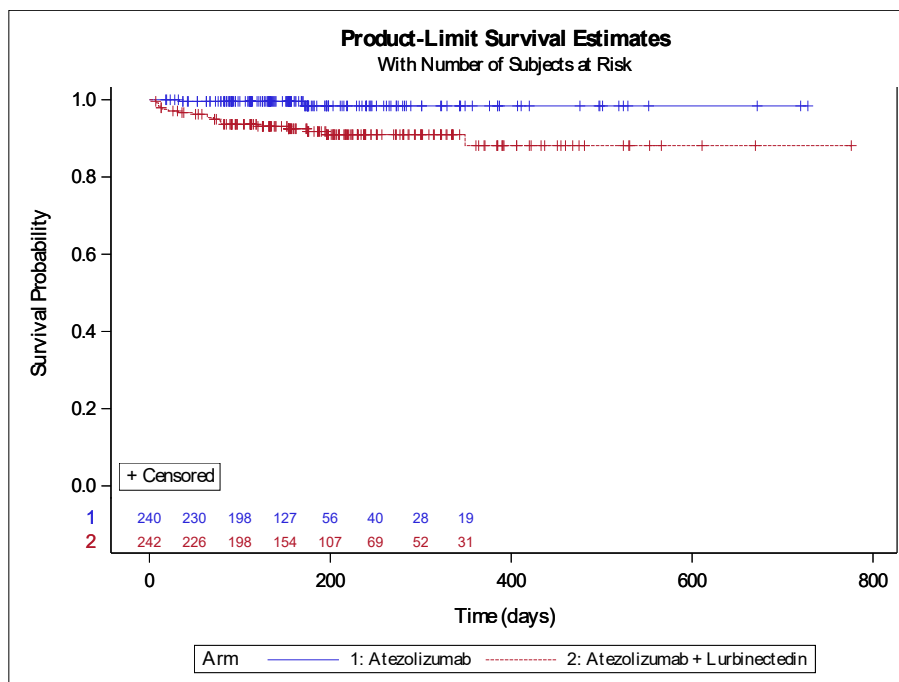


Abbildung 37: Kaplan-Meier plot for grade  $\geq 3$  AE (PT anemia), IMforte trial, Safety Analysis Set, CCOD 29 July 2024

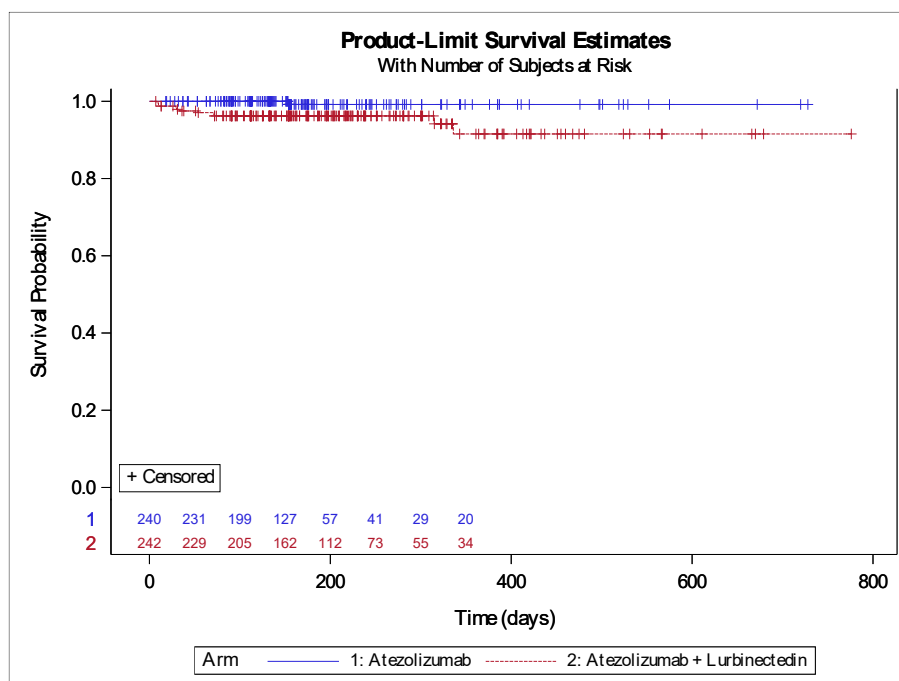


Abbildung 38: Kaplan-Meier plot for grade  $\geq 3$  AE (PT neutropenia), IMforte trial, Safety Analysis Set, CCOD 29 July 2024

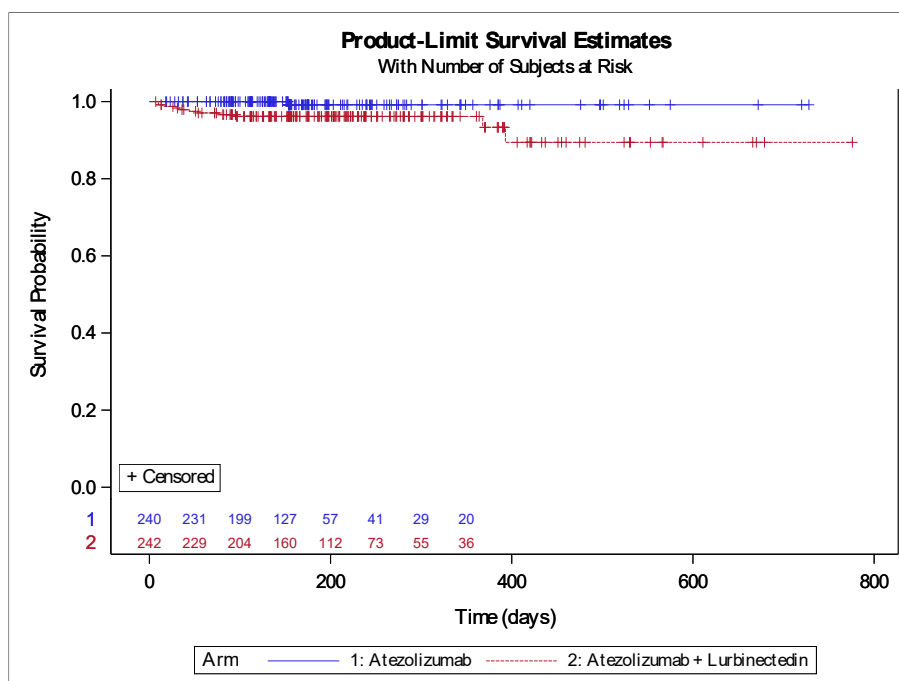


Abbildung 39: Kaplan-Meier plot for grade  $\geq 3$  AE (PT thrombocytopenia), IMforte trial, Safety Analysis Set, CCOD 29 July 2024

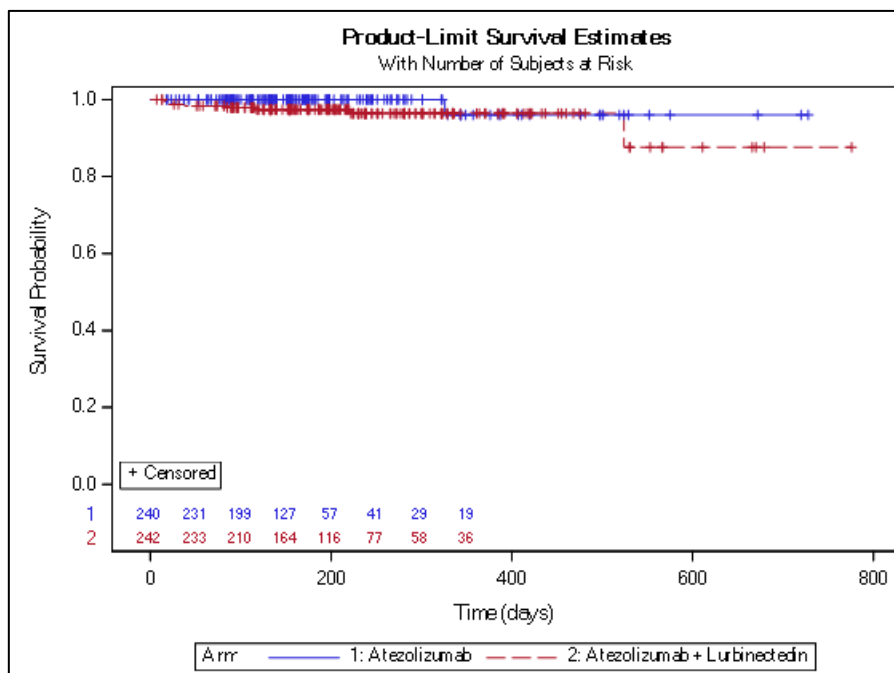


Abbildung 40: Kaplan-Meier plot for grade  $\geq 3$  AE (SOC cardiac disorders), IMforte trial, Safety Analysis Set, CCOD 29 July 2024

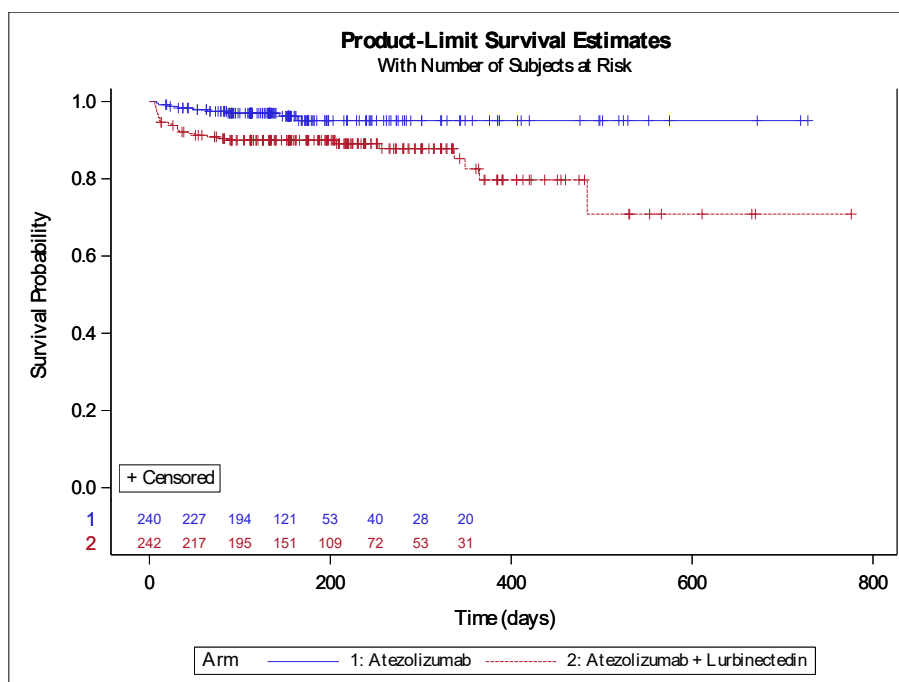


Abbildung 41: Kaplan-Meier plot for grade  $\geq 3$  AE (SOC investigations), IMforte trial, Safety Analysis Set, CCOD 29 July 2024

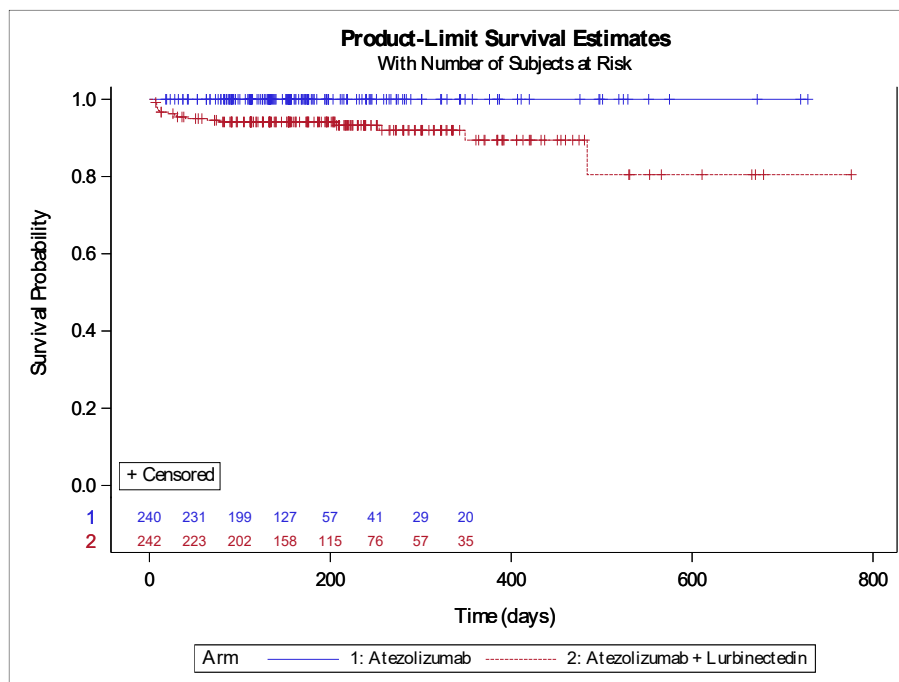


Abbildung 42: Kaplan-Meier plot for grade  $\geq 3$  AE (PT neutrophil count decreased), IMforte trial, Safety Analysis Set, CCOD 29 July 2024

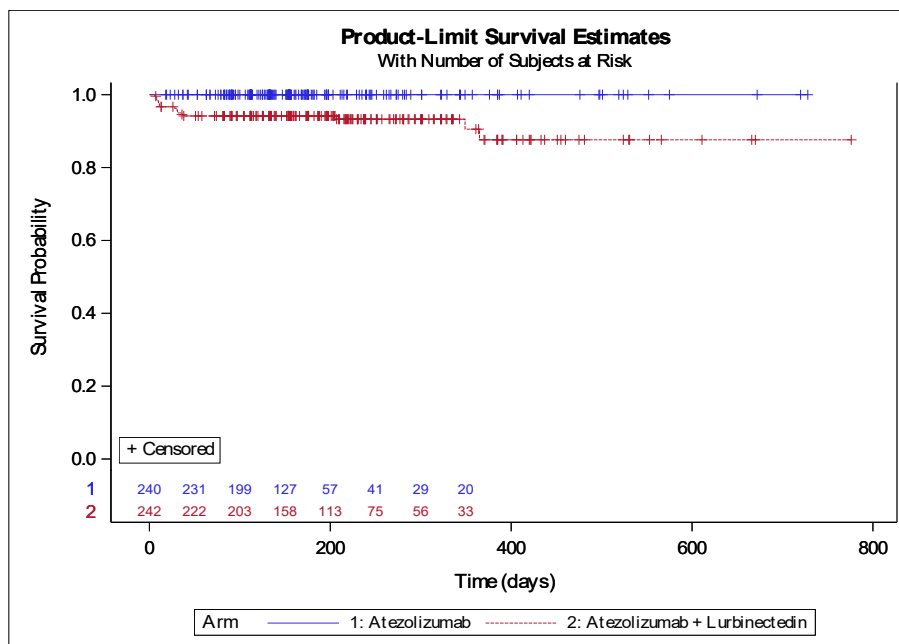


Abbildung 43: Kaplan-Meier plot for grade  $\geq 3$  AE (PT platelet count decreased), IMforte trial, Safety Analysis Set, CCOD 29 July 2024

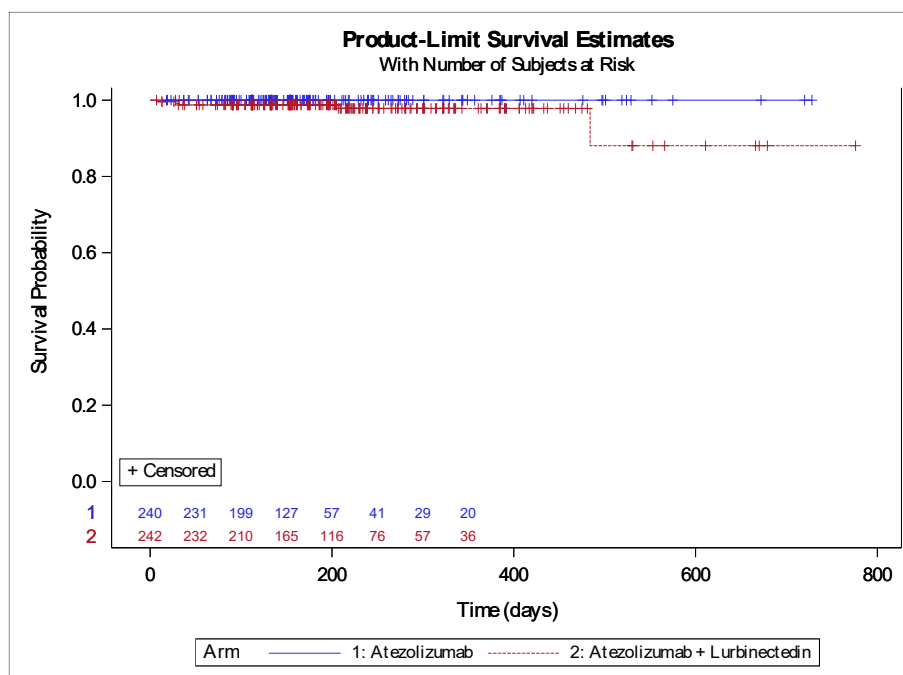


Abbildung 44: Kaplan-Meier plot for grade  $\geq 3$  AE (PT white blood cell count decreased), IMforte trial, Safety Analysis Set, CCOD 29 July 2024

Tabelle 5: Grade 5 severe AE (death related to AE) by SOC and PT including effect estimates

| Endpoint<br>SOC<br>PT                                | Lurbinectedin + atezolizumab |                                                                                                       | Atezolizumab       |                                                                                                    | Lurbinectedin + atezolizumab vs.<br>atezolizumab |
|------------------------------------------------------|------------------------------|-------------------------------------------------------------------------------------------------------|--------------------|----------------------------------------------------------------------------------------------------|--------------------------------------------------|
|                                                      | N/N <sup>Cen</sup>           | Median time to event in<br>days <sup>a</sup><br>[95% CI] <sup>b</sup><br>patients with event<br>n (%) | N/N <sup>Cen</sup> | Median time to event in days <sup>a</sup><br>[95% CI] <sup>b</sup><br>patients with event<br>n (%) | HR [95% CI] <sup>c</sup><br>p-value <sup>d</sup> |
| Blood and lymphatic system disorders                 | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [NE; NE]<br>0.3205                            |
| Febrile neutropenia                                  | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [NE; NE]<br>0.3205                            |
| Cardiac disorders                                    | 242/238                      | NE [NE; NE]<br>4 (1.7)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [NE; NE]<br>0.0801                            |
| Cardio-respiratory arrest                            | 242/240                      | NE [NE; NE]<br>2 (0.8)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [NE; NE]<br>0.1624                            |
| Myocardial infarction                                | 242/240                      | NE [NE; NE]<br>2 (0.8)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [NE; NE]<br>0.2836                            |
| General disorders and administration site conditions | 242/242                      | NE [NE; NE]<br>0 (0.0)                                                                                | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                             | NE [NE; NE]<br>0.1902                            |
| Death                                                | 242/242                      | NE [NE; NE]<br>0 (0.0)                                                                                | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                             | NE [NE; NE]<br>0.1902                            |
| Infections and infestations                          | 242/236                      | NE [NE; NE]<br>6 (2.5)                                                                                | 240/236            | NE [NE; NE]<br>4 (1.7)                                                                             | 1.31 [0.37; 4.70]<br>0.6774                      |

| Endpoint<br>SOC<br>PT           | Lurbinectedin + atezolizumab |                                                                                                       | Atezolizumab       |                                                                                                    | Lurbinectedin + atezolizumab vs.<br>atezolizumab |
|---------------------------------|------------------------------|-------------------------------------------------------------------------------------------------------|--------------------|----------------------------------------------------------------------------------------------------|--------------------------------------------------|
|                                 | N/N <sup>Cen</sup>           | Median time to event in<br>days <sup>a</sup><br>[95% CI] <sup>b</sup><br>patients with event<br>n (%) | N/N <sup>Cen</sup> | Median time to event in days <sup>a</sup><br>[95% CI] <sup>b</sup><br>patients with event<br>n (%) | HR [95% CI] <sup>c</sup><br>p-value <sup>d</sup> |
| Abscess<br>intestinal           | 242/242                      | NE [NE; NE]<br>0 (0.0)                                                                                | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                             | NE [NE; NE]<br>0.3183                            |
| COVID-19<br>pneumonia           | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [NE; NE]<br>0.3193                            |
| Pneumonia                       | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/238            | NE [NE; NE]<br>2 (0.8)                                                                             | 0.38 [0.03; 4.35]<br>0.4223                      |
| Pneumonia<br>viral              | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [NE; NE]<br>0.3193                            |
| Sepsis                          | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                             | 0.73 [0.04; 11.91]<br>0.8218                     |
| Septic shock                    | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [NE; NE]<br>0.3194                            |
| Vascular<br>device<br>infection | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [NE; NE]<br>0.3205                            |
| Nervous system<br>disorders     | 242/242                      | NE [NE; NE]<br>0 (0.0)                                                                                | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                             | NE [NE; NE]<br>0.3163                            |
| Cerebrovascu-<br>lar accident   | 242/242                      | NE [NE; NE]<br>0 (0.0)                                                                                | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                             | NE [NE; NE]<br>0.3163                            |

| Endpoint<br>SOC<br>PT                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           | Lurbinectedin + atezolizumab |                                                                                                    | Atezolizumab       |                                                                                                    | Lurbinectedin + atezolizumab vs.<br>atezolizumab |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------|----------------------------------------------------------------------------------------------------|--------------------|----------------------------------------------------------------------------------------------------|--------------------------------------------------|
|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 | N/N <sup>Cen</sup>           | Median time to event in days <sup>a</sup><br>[95% CI] <sup>b</sup><br>patients with event<br>n (%) | N/N <sup>Cen</sup> | Median time to event in days <sup>a</sup><br>[95% CI] <sup>b</sup><br>patients with event<br>n (%) | HR [95% CI] <sup>c</sup><br>p-value <sup>d</sup> |
| Psychiatric disorders                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                             | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [NE; NE]<br>0.4733                            |
| Completed suicide                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                             | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [NE; NE]<br>0.4733                            |
| CCOD: 29 July 2024; NE: not estimable.<br>a: summaries of duration (median) are Kaplan-Meier estimates.<br>b: 95% CIs for the median were computed using the method of Brookmeyer and Crowley.<br>c: hazard ratios were estimated using a stratified Cox proportional hazard model. The stratification factors are ECOG PS at randomization (0 vs. 1), LDH at randomization (≤ULN vs >ULN) via local laboratory test, presence of liver metastases at enrollment (yes vs. no), and prior receipt of PCI (yes vs. no).<br>d: p-value based on the log rank test. |                              |                                                                                                    |                    |                                                                                                    |                                                  |

Tabelle 6: Serious AE by SOC and PT including effect estimates

| Endpoint<br>SOC<br>PT                | Lurbinectedin + atezolizumab |                                                                                                    | Atezolizumab       |                                                                                                    | Lurbinectedin + atezolizumab vs.<br>atezolizumab |
|--------------------------------------|------------------------------|----------------------------------------------------------------------------------------------------|--------------------|----------------------------------------------------------------------------------------------------|--------------------------------------------------|
|                                      | N/N <sup>Cen</sup>           | Median time to event in days <sup>a</sup><br>[95% CI] <sup>b</sup><br>patients with event<br>n (%) | N/N <sup>Cen</sup> | Median time to event in days <sup>a</sup><br>[95% CI] <sup>b</sup><br>patients with event<br>n (%) | HR [95% CI] <sup>c</sup><br>p-value <sup>d</sup> |
| Blood and lymphatic system disorders | 242/234                      | NE [NE; NE]<br>8 (3.3)                                                                             | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                             | 6.99 [0.87; 55.56]<br>0.0335                     |

| Endpoint<br>SOC<br>PT          | Lurbinectedin + atezolizumab |                                                                                                    | Atezolizumab       |                                                                                                    | Lurbinectedin +<br>atezolizumab vs.<br>atezolizumab |
|--------------------------------|------------------------------|----------------------------------------------------------------------------------------------------|--------------------|----------------------------------------------------------------------------------------------------|-----------------------------------------------------|
|                                | N/N <sup>Cen</sup>           | Median time to event in days <sup>a</sup><br>[95% CI] <sup>b</sup><br>patients with event<br>n (%) | N/N <sup>Cen</sup> | Median time to event in days <sup>a</sup><br>[95% CI] <sup>b</sup><br>patients with event<br>n (%) | HR [95% CI] <sup>c</sup><br>p-value <sup>d</sup>    |
| Anemia                         | 242/240                      | NE [NE; NE]<br>2 (0.8)                                                                             | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [NE; NE]<br>0.2352                               |
| Febrile neutropenia            | 242/238                      | NE [NE; NE]<br>4 (1.7)                                                                             | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [NE; NE]<br>0.0502                               |
| Lymphadenitis                  | 242/242                      | NE [NE; NE]<br>0 (0.0)                                                                             | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                             | NE [NE; NE]<br>0.3153                               |
| Pancytopenia                   | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                             | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [NE; NE]<br>0.4268                               |
| Thrombocytopenia               | 242/240                      | NE [NE; NE]<br>2 (0.8)                                                                             | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [NE; NE]<br>0.1600                               |
| Cardiac disorders              | 242/234                      | NE [NE; NE]<br>8 (3.3)                                                                             | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                             | 6.54 [0.81; 52.63]<br>0.0425                        |
| Acute myocardial<br>infarction | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                             | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [NE; NE]<br>0.3554                               |
| Atrial fibrillation            | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                             | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [NE; NE]<br>0.3163                               |
| Cardio-respiratory<br>arrest   | 242/240                      | NE [NE; NE]<br>2 (0.8)                                                                             | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                             | 1.64 [0.15; 18.52]<br>0.6863                        |

| Endpoint<br>SOC<br>PT      | Lurbinectedin + atezolizumab |                                                                                                    | Atezolizumab       |                                                                                                    | Lurbinectedin +<br>atezolizumab vs.<br>atezolizumab |
|----------------------------|------------------------------|----------------------------------------------------------------------------------------------------|--------------------|----------------------------------------------------------------------------------------------------|-----------------------------------------------------|
|                            | N/N <sup>Cen</sup>           | Median time to event in days <sup>a</sup><br>[95% CI] <sup>b</sup><br>patients with event<br>n (%) | N/N <sup>Cen</sup> | Median time to event in days <sup>a</sup><br>[95% CI] <sup>b</sup><br>patients with event<br>n (%) | HR [95% CI] <sup>c</sup><br>p-value <sup>d</sup>    |
| Myocardial infarction      | 242/239                      | NE [NE; NE]<br>3 (1.2)                                                                             | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [NE; NE]<br>0.1460                               |
| Palpitations               | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                             | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [NE; NE]<br>0.3566                               |
| Endocrine disorders        | 242/242                      | NE [NE; NE]<br>0 (0.0)                                                                             | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                             | NE [NE; NE]<br>0.3131                               |
| Adrenal insufficiency      | 242/242                      | NE [NE; NE]<br>0 (0.0)                                                                             | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                             | NE [NE; NE]<br>0.3131                               |
| Gastrointestinal disorders | 242/234                      | NE [NE; NE]<br>8 (3.3)                                                                             | 240/230            | NE [NE; NE]<br>10 (4.2)                                                                            | 0.73 [0.29; 1.85]<br>0.4970                         |
| Abdominal pain             | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                             | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [NE; NE]<br>0.4332                               |
| Abdominal pain upper       | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                             | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [NE; NE]<br>0.3183                               |
| Chronic gastritis          | 242/242                      | NE [NE; NE]<br>0 (0.0)                                                                             | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                             | NE [NE; NE]<br>0.2130                               |
| Colitis                    | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                             | 240/238            | NE [NE; NE]<br>2 (0.8)                                                                             | 0.47 [0.04; 5.21]<br>0.5298                         |

| Endpoint<br>SOC<br>PT                                      | Lurbinectedin + atezolizumab |                                                                                                    | Atezolizumab       |                                                                                                    | Lurbinectedin +<br>atezolizumab vs.<br>atezolizumab |
|------------------------------------------------------------|------------------------------|----------------------------------------------------------------------------------------------------|--------------------|----------------------------------------------------------------------------------------------------|-----------------------------------------------------|
|                                                            | N/N <sup>Cen</sup>           | Median time to event in days <sup>a</sup><br>[95% CI] <sup>b</sup><br>patients with event<br>n (%) | N/N <sup>Cen</sup> | Median time to event in days <sup>a</sup><br>[95% CI] <sup>b</sup><br>patients with event<br>n (%) | HR [95% CI] <sup>c</sup><br>p-value <sup>d</sup>    |
| Constipation                                               | 242/240                      | NE [NE; NE]<br>2 (0.8)                                                                             | 240/238            | NE [NE; NE]<br>2 (0.8)                                                                             | 0.99 [0.14; 6.99]<br>0.9885                         |
| Gastrointestinal<br>hemorrhage                             | 242/242                      | NE [NE; NE]<br>0 (0.0)                                                                             | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                             | NE [NE; NE]<br>0.3110                               |
| Gastrointestinal<br>polyp hemorrhage                       | 242/242                      | NE [NE; NE]<br>0 (0.0)                                                                             | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                             | NE [NE; NE]<br>0.1824                               |
| Ileus                                                      | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                             | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [NE; NE]<br>0.3193                               |
| Intestinal<br>obstruction                                  | 242/242                      | NE [NE; NE]<br>0 (0.0)                                                                             | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                             | NE [NE; NE]<br>0.3153                               |
| Nausea                                                     | 242/240                      | NE [NE; NE]<br>2 (0.8)                                                                             | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                             | 1.98 [0.18; 21.74]<br>0.5695                        |
| Pancreatitis acute                                         | 242/242                      | NE [NE; NE]<br>0 (0.0)                                                                             | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                             | NE [NE; NE]<br>0.3152                               |
| Volvulus                                                   | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                             | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                             | 0.75 [0.05; 12.35]<br>0.8410                        |
| General disorders and<br>administration site<br>conditions | 242/234                      | NE [NE; NE]<br>8 (3.3)                                                                             | 240/237            | NE [NE; NE]<br>3 (1.3)                                                                             | 2.17 [0.57; 8.26]<br>0.2460                         |

| Endpoint<br>SOC<br>PT                | Lurbinectedin + atezolizumab |                                                                                                    | Atezolizumab       |                                                                                                    | Lurbinectedin +<br>atezolizumab vs.<br>atezolizumab |
|--------------------------------------|------------------------------|----------------------------------------------------------------------------------------------------|--------------------|----------------------------------------------------------------------------------------------------|-----------------------------------------------------|
|                                      | N/N <sup>Cen</sup>           | Median time to event in days <sup>a</sup><br>[95% CI] <sup>b</sup><br>patients with event<br>n (%) | N/N <sup>Cen</sup> | Median time to event in days <sup>a</sup><br>[95% CI] <sup>b</sup><br>patients with event<br>n (%) | HR [95% CI] <sup>c</sup><br>p-value <sup>d</sup>    |
| Adhesion                             | 242/242                      | NE [NE; NE]<br>0 (0.0)                                                                             | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                             | NE [NE; NE]<br>0.1654                               |
| Administration site<br>extravasation | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                             | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [NE; NE]<br>0.3183                               |
| Chest pain                           | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                             | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                             | 0.69 [0.04; 11.49]<br>0.7919                        |
| Death                                | 242/242                      | NE [NE; NE]<br>0 (0.0)                                                                             | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                             | NE [NE; NE]<br>0.1902                               |
| Fatigue                              | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                             | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [NE; NE]<br>0.3194                               |
| Oedema peripheral                    | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                             | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [NE; NE]<br>0.4727                               |
| Pain                                 | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                             | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [NE; NE]<br>0.3205                               |
| Pyrexia                              | 242/239                      | NE [NE; NE]<br>3 (1.2)                                                                             | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [NE; NE]<br>0.0837                               |
| Hepatobiliary<br>disorders           | 242/240                      | NE [NE; NE]<br>2 (0.8)                                                                             | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [NE; NE]<br>0.1623                               |

| Endpoint<br>SOC<br>PT          | Lurbinectedin + atezolizumab |                                                                                                    | Atezolizumab       |                                                                                                    | Lurbinectedin +<br>atezolizumab vs.<br>atezolizumab |
|--------------------------------|------------------------------|----------------------------------------------------------------------------------------------------|--------------------|----------------------------------------------------------------------------------------------------|-----------------------------------------------------|
|                                | N/N <sup>Cen</sup>           | Median time to event in days <sup>a</sup><br>[95% CI] <sup>b</sup><br>patients with event<br>n (%) | N/N <sup>Cen</sup> | Median time to event in days <sup>a</sup><br>[95% CI] <sup>b</sup><br>patients with event<br>n (%) | HR [95% CI] <sup>c</sup><br>p-value <sup>d</sup>    |
| Cholecystitis                  | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                             | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [NE; NE]<br>0.3237                               |
| Immune-mediated<br>hepatitis   | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                             | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [NE; NE]<br>0.3237                               |
| Infections and<br>infestations | 242/217                      | NE [NE; NE]<br>25 (10.3)                                                                           | 240/224            | NE [NE; NE]<br>16 (6.7)                                                                            | 1.36 [0.72; 2.56]<br>0.3389                         |
| Abscess intestinal             | 242/242                      | NE [NE; NE]<br>0 (0.0)                                                                             | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                             | NE [NE; NE]<br>0.3183                               |
| Bacteroides<br>infection       | 242/242                      | NE [NE; NE]<br>0 (0.0)                                                                             | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                             | NE [NE; NE]<br>0.3183                               |
| Bursitis infective             | 242/242                      | NE [NE; NE]<br>0 (0.0)                                                                             | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                             | NE [NE; NE]<br>0.1994                               |
| COVID-19                       | 242/240                      | NE [NE; NE]<br>2 (0.8)                                                                             | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                             | 1.97 [0.18; 21.74]<br>0.5729                        |
| COVID-19<br>pneumonia          | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                             | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [NE; NE]<br>0.3193                               |
| Cellulitis                     | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                             | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [NE; NE]<br>0.3204                               |

| Endpoint<br>SOC<br>PT                | Lurbinectedin + atezolizumab |                                                                                                    | Atezolizumab       |                                                                                                    | Lurbinectedin +<br>atezolizumab vs.<br>atezolizumab |
|--------------------------------------|------------------------------|----------------------------------------------------------------------------------------------------|--------------------|----------------------------------------------------------------------------------------------------|-----------------------------------------------------|
|                                      | N/N <sup>Cen</sup>           | Median time to event in days <sup>a</sup><br>[95% CI] <sup>b</sup><br>patients with event<br>n (%) | N/N <sup>Cen</sup> | Median time to event in days <sup>a</sup><br>[95% CI] <sup>b</sup><br>patients with event<br>n (%) | HR [95% CI] <sup>c</sup><br>p-value <sup>d</sup>    |
| Encephalitis                         | 242/242                      | NE [NE; NE]<br>0 (0.0)                                                                             | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                             | NE [NE; NE]<br>0.2816                               |
| Febrile infection                    | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                             | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [NE; NE]<br>0.3258                               |
| Infection                            | 242/239                      | NE [NE; NE]<br>3 (1.2)                                                                             | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [NE; NE]<br>0.0839                               |
| Lower respiratory<br>tract infection | 242/240                      | NE [NE; NE]<br>2 (0.8)                                                                             | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                             | 1.96 [0.18; 21.74]<br>0.5747                        |
| Pharyngitis                          | 242/242                      | NE [NE; NE]<br>0 (0.0)                                                                             | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                             | NE [NE; NE]<br>0.2820                               |
| Pneumocystis<br>jirovecii pneumonia  | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                             | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [NE; NE]<br>0.3183                               |
| Pneumonia                            | 242/236                      | NE [NE; NE]<br>6 (2.5)                                                                             | 240/234            | NE [NE; NE]<br>6 (2.5)                                                                             | 0.86 [0.27; 2.68]<br>0.7894                         |
| Pneumonia viral                      | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                             | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [NE; NE]<br>0.3193                               |
| Respiratory tract<br>infection       | 242/237                      | NE [NE; NE]<br>5 (2.1)                                                                             | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                             | 3.51 [0.41; 30.30]<br>0.2245                        |

| Endpoint<br>SOC<br>PT                                | Lurbinectedin + atezolizumab |                                                                                                    | Atezolizumab       |                                                                                                    | Lurbinectedin +<br>atezolizumab vs.<br>atezolizumab |
|------------------------------------------------------|------------------------------|----------------------------------------------------------------------------------------------------|--------------------|----------------------------------------------------------------------------------------------------|-----------------------------------------------------|
|                                                      | N/N <sup>Cen</sup>           | Median time to event in days <sup>a</sup><br>[95% CI] <sup>b</sup><br>patients with event<br>n (%) | N/N <sup>Cen</sup> | Median time to event in days <sup>a</sup><br>[95% CI] <sup>b</sup><br>patients with event<br>n (%) | HR [95% CI] <sup>c</sup><br>p-value <sup>d</sup>    |
| Sepsis                                               | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                             | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                             | 0.73 [0.04; 11.91]<br>0.8218                        |
| Septic shock                                         | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                             | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [NE; NE]<br>0.3194                               |
| Urinary tract<br>infection                           | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                             | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                             | 0.87 [0.05; 13.89]<br>0.9187                        |
| Vascular device<br>infection                         | 242/240                      | NE [NE; NE]<br>2 (0.8)                                                                             | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [NE; NE]<br>0.2238                               |
| Injury, poisoning and<br>procedural<br>complications | 242/240                      | NE [NE; NE]<br>2 (0.8)                                                                             | 240/238            | NE [NE; NE]<br>2 (0.8)                                                                             | 0.69 [0.10; 5.05]<br>0.7157                         |
| Ankle fracture                                       | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                             | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [NE; NE]<br>0.4778                               |
| Fall                                                 | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                             | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [NE; NE]<br>0.4736                               |
| Femur fracture                                       | 242/242                      | NE [NE; NE]<br>0 (0.0)                                                                             | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                             | NE [NE; NE]<br>0.3153                               |
| Road traffic<br>accident                             | 242/242                      | NE [NE; NE]<br>0 (0.0)                                                                             | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                             | NE [NE; NE]<br>0.3024                               |

| Endpoint<br>SOC<br>PT                        | Lurbinectedin + atezolizumab |                                                                                                    | Atezolizumab       |                                                                                                    | Lurbinectedin +<br>atezolizumab vs.<br>atezolizumab |
|----------------------------------------------|------------------------------|----------------------------------------------------------------------------------------------------|--------------------|----------------------------------------------------------------------------------------------------|-----------------------------------------------------|
|                                              | N/N <sup>Cen</sup>           | Median time to event in days <sup>a</sup><br>[95% CI] <sup>b</sup><br>patients with event<br>n (%) | N/N <sup>Cen</sup> | Median time to event in days <sup>a</sup><br>[95% CI] <sup>b</sup><br>patients with event<br>n (%) | HR [95% CI] <sup>c</sup><br>p-value <sup>d</sup>    |
| Investigations                               | 242/236                      | NE [NE; NE]<br>6 (2.5)                                                                             | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                             | 5.56 [0.67; 45.46]<br>0.0740                        |
| Alanine<br>aminotransferase<br>increased     | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                             | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [NE; NE]<br>0.3194                               |
| Aspartate<br>aminotransferase<br>increased   | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                             | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [NE; NE]<br>0.3194                               |
| Blood bilirubin<br>increased                 | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                             | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [NE; NE]<br>0.3258                               |
| Blood creatine<br>phosphokinase<br>increased | 242/242                      | NE [NE; NE]<br>0 (0.0)                                                                             | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                             | NE [NE; NE]<br>0.3110                               |
| Lymphocyte count<br>decreased                | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                             | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [NE; NE]<br>0.3183                               |
| Neutrophil count<br>decreased                | 242/240                      | NE [NE; NE]<br>2 (0.8)                                                                             | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [NE; NE]<br>0.1577                               |
| Platelet count<br>decreased                  | 242/237                      | NE [NE; NE]<br>5 (2.1)                                                                             | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [NE; NE]<br>0.0345                               |
| White blood cell<br>count decreased          | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                             | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [NE; NE]<br>0.3183                               |

| Endpoint<br>SOC<br>PT                                 | Lurbinectedin + atezolizumab |                                                                                                    | Atezolizumab       |                                                                                                    | Lurbinectedin +<br>atezolizumab vs.<br>atezolizumab |
|-------------------------------------------------------|------------------------------|----------------------------------------------------------------------------------------------------|--------------------|----------------------------------------------------------------------------------------------------|-----------------------------------------------------|
|                                                       | N/N <sup>Cen</sup>           | Median time to event in days <sup>a</sup><br>[95% CI] <sup>b</sup><br>patients with event<br>n (%) | N/N <sup>Cen</sup> | Median time to event in days <sup>a</sup><br>[95% CI] <sup>b</sup><br>patients with event<br>n (%) | HR [95% CI] <sup>c</sup><br>p-value <sup>d</sup>    |
| Metabolism and<br>nutrition disorders                 | 242/238                      | NE [NE; NE]<br>4 (1.7)                                                                             | 240/237            | NE [NE; NE]<br>3 (1.3)                                                                             | 1.22 [0.27; 5.50]<br>0.7918                         |
| Acidosis                                              | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                             | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [NE; NE]<br>0.3260                               |
| Alkalosis                                             | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                             | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [NE; NE]<br>0.3258                               |
| Diabetic<br>ketoacidosis                              | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                             | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [NE; NE]<br>0.3194                               |
| Hyponatremia                                          | 242/240                      | NE [NE; NE]<br>2 (0.8)                                                                             | 240/237            | NE [NE; NE]<br>3 (1.3)                                                                             | 0.59 [0.10; 3.57]<br>0.5626                         |
| Musculoskeletal and<br>connective tissue<br>disorders | 242/238                      | NE [NE; NE]<br>4 (1.7)                                                                             | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                             | 3.22 [0.36; 29.41]<br>0.2731                        |
| Arthralgia                                            | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                             | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [NE; NE]<br>0.4692                               |
| Back pain                                             | 242/240                      | NE [NE; NE]<br>2 (0.8)                                                                             | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [NE; NE]<br>0.1586                               |
| Mobility decreased                                    | 242/242                      | NE [NE; NE]<br>0 (0.0)                                                                             | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                             | NE [NE; NE]<br>0.3132                               |

| Endpoint<br>SOC<br>PT                                                        | Lurbinectedin + atezolizumab |                                                                                                    | Atezolizumab       |                                                                                                    | Lurbinectedin +<br>atezolizumab vs.<br>atezolizumab |
|------------------------------------------------------------------------------|------------------------------|----------------------------------------------------------------------------------------------------|--------------------|----------------------------------------------------------------------------------------------------|-----------------------------------------------------|
|                                                                              | N/N <sup>Cen</sup>           | Median time to event in days <sup>a</sup><br>[95% CI] <sup>b</sup><br>patients with event<br>n (%) | N/N <sup>Cen</sup> | Median time to event in days <sup>a</sup><br>[95% CI] <sup>b</sup><br>patients with event<br>n (%) | HR [95% CI] <sup>c</sup><br>p-value <sup>d</sup>    |
| Pain in extremity                                                            | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                             | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [NE; NE]<br>0.4475                               |
| Neoplasms benign,<br>malignant and<br>unspecified (incl<br>cysts and polyps) | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                             | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                             | 0.72 [0.04; 11.63]<br>0.8133                        |
| Acute myeloid<br>leukemia                                                    | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                             | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [NE; NE]<br>0.4386                               |
| Prostate cancer                                                              | 242/242                      | NE [NE; NE]<br>0 (0.0)                                                                             | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                             | NE [NE; NE]<br>0.2795                               |
| Nervous system<br>disorders                                                  | 242/237                      | NE [NE; NE]<br>5 (2.1)                                                                             | 240/235            | NE [NE; NE]<br>5 (2.1)                                                                             | 0.72 [0.21; 2.52]<br>0.6048                         |
| Cerebrovascular<br>accident                                                  | 242/242                      | NE [NE; NE]<br>0 (0.0)                                                                             | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                             | NE [NE; NE]<br>0.3163                               |
| Dizziness                                                                    | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                             | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [NE; NE]<br>0.4475                               |
| Neuropathy<br>peripheral                                                     | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                             | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                             | 0.98 [0.06; 15.63]<br>0.9903                        |

| Endpoint<br>SOC<br>PT          | Lurbinectedin + atezolizumab |                                                                                                    | Atezolizumab       |                                                                                                    | Lurbinectedin +<br>atezolizumab vs.<br>atezolizumab |
|--------------------------------|------------------------------|----------------------------------------------------------------------------------------------------|--------------------|----------------------------------------------------------------------------------------------------|-----------------------------------------------------|
|                                | N/N <sup>Cen</sup>           | Median time to event in days <sup>a</sup><br>[95% CI] <sup>b</sup><br>patients with event<br>n (%) | N/N <sup>Cen</sup> | Median time to event in days <sup>a</sup><br>[95% CI] <sup>b</sup><br>patients with event<br>n (%) | HR [95% CI] <sup>c</sup><br>p-value <sup>d</sup>    |
| Seizure                        | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                             | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                             | 0.52 [0.03; 8.26]<br>0.6347                         |
| Syncope                        | 242/240                      | NE [NE; NE]<br>2 (0.8)                                                                             | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [NE; NE]<br>0.2925                               |
| Transient ischemic<br>attack   | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                             | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                             | 0.69 [0.04; 1.63]<br>0.7973                         |
| Psychiatric disorders          | 242/240                      | NE [NE; NE]<br>2 (0.8)                                                                             | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                             | 1.29 [0.11; 14.71]<br>0.8367                        |
| Completed suicide              | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                             | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [NE; NE]<br>0.4733                               |
| Confusional state              | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                             | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [NE; NE]<br>0.3204                               |
| Delirium                       | 242/242                      | NE [NE; NE]<br>0 (0.0)                                                                             | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                             | NE [NE; NE]<br>0.1654                               |
| Renal and urinary<br>disorders | 242/236                      | NE [NE; NE]<br>6 (2.5)                                                                             | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [NE; NE]<br>0.0385                               |
| Acute kidney injury            | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                             | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [NE; NE]<br>0.3810                               |

| Endpoint<br>SOC<br>PT                                 | Lurbinectedin + atezolizumab |                                                                                                    | Atezolizumab       |                                                                                                    | Lurbinectedin +<br>atezolizumab vs.<br>atezolizumab |
|-------------------------------------------------------|------------------------------|----------------------------------------------------------------------------------------------------|--------------------|----------------------------------------------------------------------------------------------------|-----------------------------------------------------|
|                                                       | N/N <sup>Cen</sup>           | Median time to event in days <sup>a</sup><br>[95% CI] <sup>b</sup><br>patients with event<br>n (%) | N/N <sup>Cen</sup> | Median time to event in days <sup>a</sup><br>[95% CI] <sup>b</sup><br>patients with event<br>n (%) | HR [95% CI] <sup>c</sup><br>p-value <sup>d</sup>    |
| Immune-mediated<br>nephritis                          | 242/240                      | NE [NE; NE]<br>2 (0.8)                                                                             | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [NE; NE]<br>0.2781                               |
| Nephropathy                                           | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                             | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [NE; NE]<br>0.3183                               |
| Perinephric<br>collection                             | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                             | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [NE; NE]<br>0.4682                               |
| Renal failure                                         | 242/240                      | NE [NE; NE]<br>2 (0.8)                                                                             | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [NE; NE]<br>0.2264                               |
| Respiratory, thoracic<br>and mediastinal<br>disorders | 242/229                      | NE [NE; NE]<br>13 (5.4)                                                                            | 240/234            | NE [NE; NE]<br>6 (2.5)                                                                             | 1.98 [0.75; 5.21]<br>0.1617                         |
| Asthma                                                | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                             | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [NE; NE]<br>0.3193                               |
| Bronchospasm                                          | 242/242                      | NE [NE; NE]<br>0 (0.0)                                                                             | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                             | NE [NE; NE]<br>0.3163                               |
| Dyspnea                                               | 242/237                      | NE [NE; NE]<br>5 (2.1)                                                                             | 240/236            | NE [NE; NE]<br>4 (1.7)                                                                             | 1.08 [0.29; 4.07]<br>0.9111                         |
| Hemoptysis                                            | 242/240                      | NE [NE; NE]<br>2 (0.8)                                                                             | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                             | 1.67 [0.15; 18.87]<br>0.6734                        |

| Endpoint<br>SOC<br>PT                  | Lurbinectedin + atezolizumab |                                                                                                    | Atezolizumab       |                                                                                                    | Lurbinectedin +<br>atezolizumab vs.<br>atezolizumab |
|----------------------------------------|------------------------------|----------------------------------------------------------------------------------------------------|--------------------|----------------------------------------------------------------------------------------------------|-----------------------------------------------------|
|                                        | N/N <sup>Cen</sup>           | Median time to event in days <sup>a</sup><br>[95% CI] <sup>b</sup><br>patients with event<br>n (%) | N/N <sup>Cen</sup> | Median time to event in days <sup>a</sup><br>[95% CI] <sup>b</sup><br>patients with event<br>n (%) | HR [95% CI] <sup>c</sup><br>p-value <sup>d</sup>    |
| Immune-mediated lung disease           | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                             | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [NE; NE]<br>0.3193                               |
| Pleural effusion                       | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                             | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [NE; NE]<br>0.3541                               |
| Pneumonitis                            | 242/240                      | NE [NE; NE]<br>2 (0.8)                                                                             | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [NE; NE]<br>0.1595                               |
| Productive cough                       | 242/242                      | NE [NE; NE]<br>0 (0.0)                                                                             | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                             | NE [NE; NE]<br>0.1482                               |
| Pulmonary embolism                     | 242/240                      | NE [NE; NE]<br>2 (0.8)                                                                             | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [NE; NE]<br>0.1748                               |
| Respiratory failure                    | 242/240                      | NE [NE; NE]<br>2 (0.8)                                                                             | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [NE; NE]<br>0.1623                               |
| Skin and subcutaneous tissue disorders | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                             | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [NE; NE]<br>0.3237                               |
| Panniculitis                           | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                             | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [NE; NE]<br>0.3237                               |
| Vascular disorders                     | 242/238                      | NE [NE; NE]<br>4 (1.7)                                                                             | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [NE; NE]<br>0.0700                               |

| Endpoint<br>SOC<br>PT                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | Lurbinectedin + atezolizumab |                                                                                                    | Atezolizumab       |                                                                                                    | Lurbinectedin +<br>atezolizumab vs.<br>atezolizumab |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------|----------------------------------------------------------------------------------------------------|--------------------|----------------------------------------------------------------------------------------------------|-----------------------------------------------------|
|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           | N/N <sup>Cen</sup>           | Median time to event in days <sup>a</sup><br>[95% CI] <sup>b</sup><br>patients with event<br>n (%) | N/N <sup>Cen</sup> | Median time to event in days <sup>a</sup><br>[95% CI] <sup>b</sup><br>patients with event<br>n (%) | HR [95% CI] <sup>c</sup><br>p-value <sup>d</sup>    |
| Arteriosclerosis                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                             | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [NE; NE]<br>0.4475                               |
| Superior vena cava<br>syndrome                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                             | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [NE; NE]<br>0.3827                               |
| Thrombophlebitis                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                             | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [NE; NE]<br>0.3314                               |
| Thrombosis                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                             | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [NE; NE]<br>0.3194                               |
| CCOD: 29 July 2024; NE: not estimable.<br>a: summaries of duration (median) are Kaplan-Meier estimates.<br>b: 95% CIs for the median were computed using the method of Brookmeyer and Crowley.<br>c: hazard ratios were estimated using a stratified Cox proportional hazard model. The stratification factors are ECOG PS at randomization (0 vs. 1), LDH at randomization ( $\leq$ ULN vs $>$ ULN) via local laboratory test, presence of liver metastases at enrollment (yes vs. no), and prior receipt of PCI (yes vs. no).<br>d: p-value based on the log rank test. |                              |                                                                                                    |                    |                                                                                                    |                                                     |

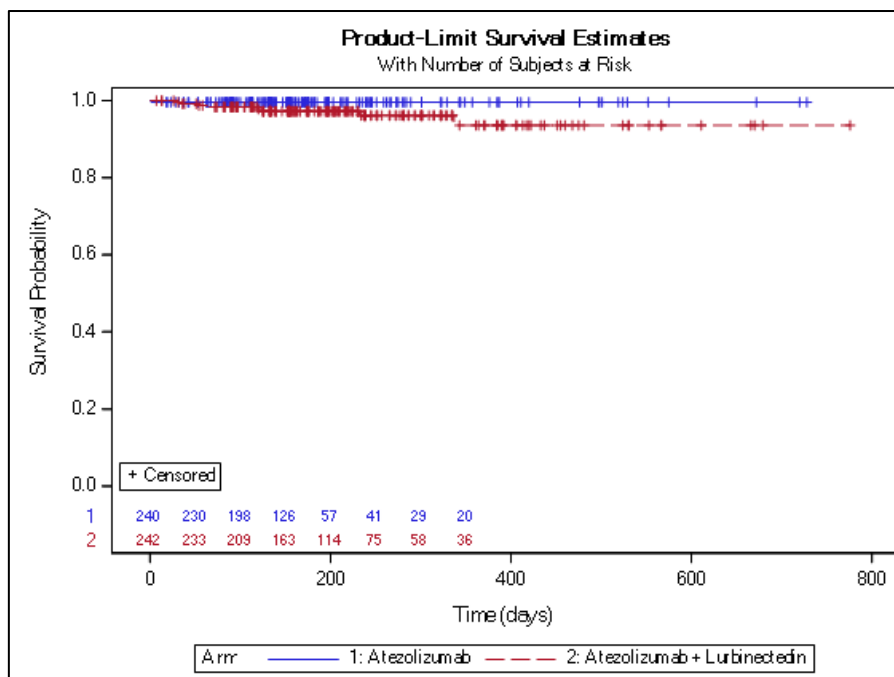


Abbildung 45: Kaplan-Meier plot for serious AE (SOC blood and lymphatic system disorders), IMforte trial, Safety Analysis Set, CCOD 29 July 2024

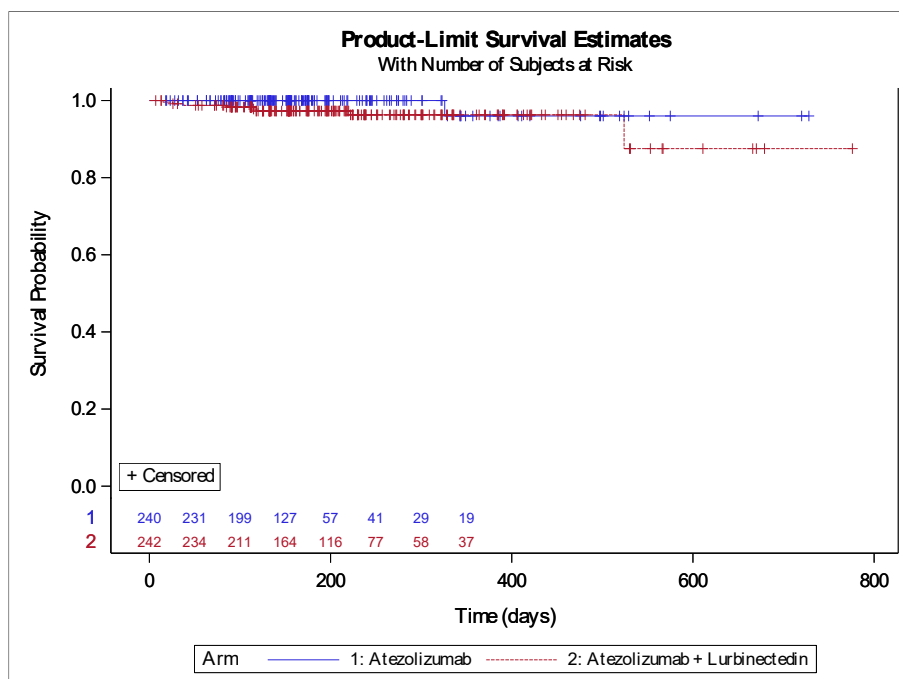


Abbildung 46: Kaplan-Meier plot for serious AE (SOC cardiac disorders), IMforte trial, Safety Analysis Set, CCOD 29 July 2024

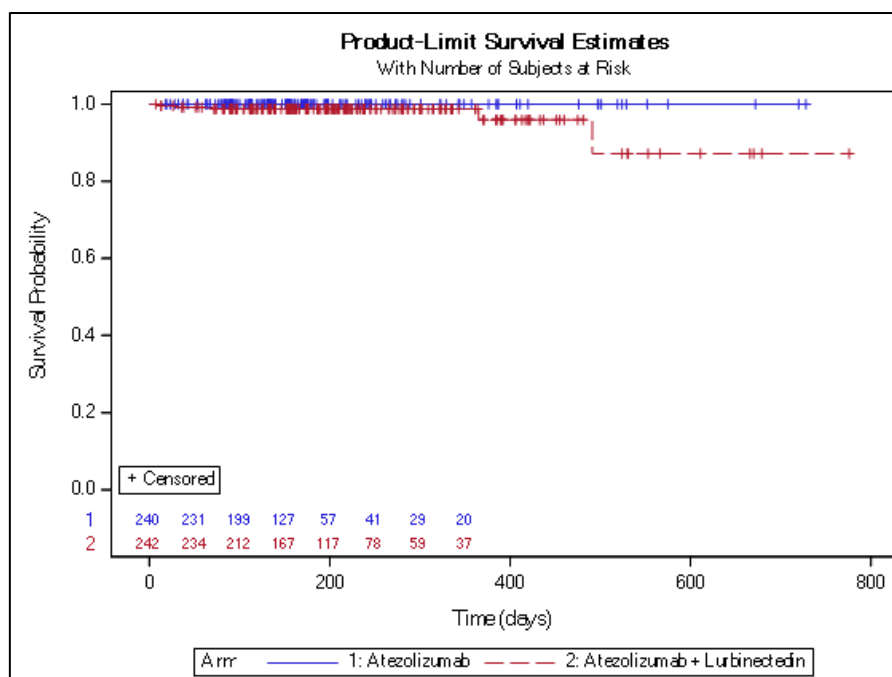


Abbildung 47: Kaplan-Meier plot for serious AE (PT platelet count decreased), IMforte trial, Safety Analysis Set, CCOD 29 July 2024

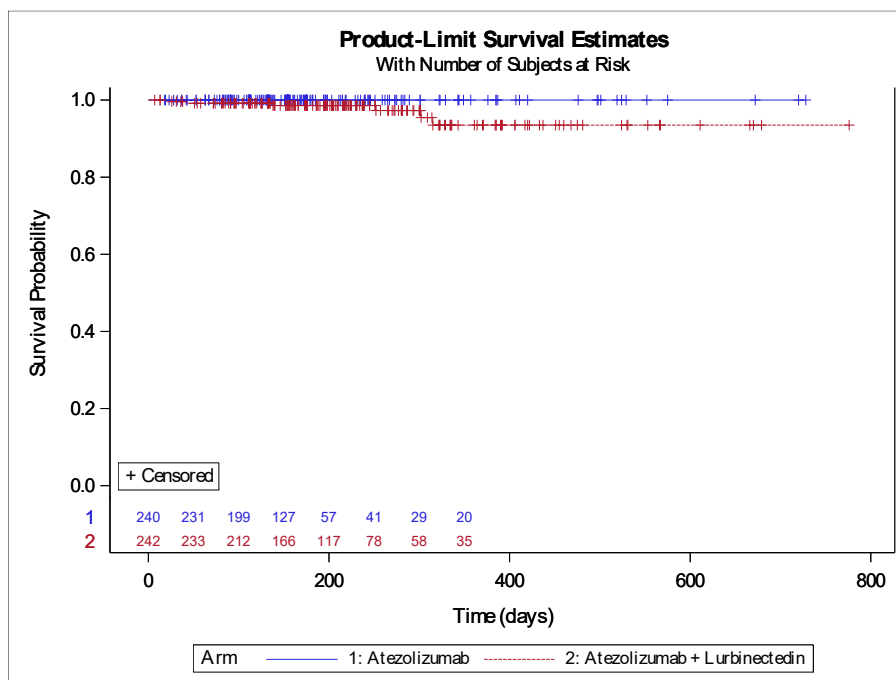


Abbildung 48: Kaplan-Meier plot for serious AE (SOC renal and urinary disorders), IMforte trial, Safety Analysis Set, CCOD 29 July 2024

Tabelle 7: Treatment discontinuation due to AE by SOC and PT including effect estimates

| Endpoint<br>SOC<br>PT                                | Lurbinectedin + atezolizumab |                                                                                                       | Atezolizumab       |                                                                                                       | Lurbinectedin + atezolizumab vs.<br>atezolizumab |
|------------------------------------------------------|------------------------------|-------------------------------------------------------------------------------------------------------|--------------------|-------------------------------------------------------------------------------------------------------|--------------------------------------------------|
|                                                      | N/N <sup>Cen</sup>           | Median time to event in<br>days <sup>a</sup><br>[95% CI] <sup>b</sup><br>patients with event<br>n (%) | N/N <sup>Cen</sup> | Median time to event in<br>days <sup>a</sup><br>[95% CI] <sup>b</sup><br>patients with event<br>n (%) | HR [95% CI] <sup>c</sup><br>p-value <sup>d</sup> |
| Blood and lymphatic system disorders                 | 242/239                      | NE [NE; NE]<br>3 (1.2)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                                | NE [NE; NE]<br>0.1103                            |
| Anemia                                               | 242/239                      | NE [NE; NE]<br>3 (1.2)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                                | NE [NE; NE]<br>0.1103                            |
| Neutropenia                                          | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                                | NE [NE; NE]<br>0.4475                            |
| Thrombocytopenia                                     | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                                | NE [NE; NE]<br>0.4475                            |
| Gastrointestinal disorders                           | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                                | 0.99 [0.06; 5.87]<br>0.9915                      |
| Gastrointestinal hemorrhage                          | 242/242                      | NE [NE; NE]<br>0 (0.0)                                                                                | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                                | NE [NE; NE]<br>0.3110                            |
| Nausea                                               | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                                | NE [NE; NE]<br>0.3193                            |
| General disorders and administration site conditions | 242/239                      | NE [NE; NE]<br>3 (1.2)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                                | NE [NE; NE]<br>0.0848                            |

| Endpoint<br>SOC<br>PT                  | Lurbinectedin + atezolizumab |                                                                                                       | Atezolizumab       |                                                                                                       | Lurbinectedin + atezolizumab vs.<br>atezolizumab |
|----------------------------------------|------------------------------|-------------------------------------------------------------------------------------------------------|--------------------|-------------------------------------------------------------------------------------------------------|--------------------------------------------------|
|                                        | N/N <sup>Cen</sup>           | Median time to event in<br>days <sup>a</sup><br>[95% CI] <sup>b</sup><br>patients with event<br>n (%) | N/N <sup>Cen</sup> | Median time to event in<br>days <sup>a</sup><br>[95% CI] <sup>b</sup><br>patients with event<br>n (%) | HR [95% CI] <sup>c</sup><br>p-value <sup>d</sup> |
| Fatigue                                | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                                | NE [NE; NE]<br>0.3193                            |
| Malaise                                | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                                | NE [NE; NE]<br>0.3193                            |
| Peripheral<br>swelling                 | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                                | NE [NE; NE]<br>0.3237                            |
| Infections and<br>infestations         | 242/242                      | NE [NE; NE]<br>0 (0.0)                                                                                | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                                | NE [NE; NE]<br>0.3163                            |
| Pneumonia                              | 242/242                      | NE [NE; NE]<br>0 (0.0)                                                                                | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                                | NE [NE; NE]<br>0.3163                            |
| Investigations                         | 242/239                      | NE [NE; NE]<br>3 (1.2)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                                | NE [NE; NE]<br>0.1120                            |
| Neutrophil<br>count decreased          | 242/239                      | NE [NE; NE]<br>3 (1.2)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                                | NE [NE; NE]<br>0.1141                            |
| Platelet count<br>decreased            | 242/240                      | NE [NE; NE]<br>2 (0.8)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                                | NE [NE; NE]<br>0.2144                            |
| White blood<br>cell count<br>decreased | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                                | NE [NE; NE]<br>0.4622                            |

| Endpoint<br>SOC<br>PT                                 | Lurbinectedin + atezolizumab |                                                                                                       | Atezolizumab       |                                                                                                       | Lurbinectedin + atezolizumab vs.<br>atezolizumab |
|-------------------------------------------------------|------------------------------|-------------------------------------------------------------------------------------------------------|--------------------|-------------------------------------------------------------------------------------------------------|--------------------------------------------------|
|                                                       | N/N <sup>Cen</sup>           | Median time to event in<br>days <sup>a</sup><br>[95% CI] <sup>b</sup><br>patients with event<br>n (%) | N/N <sup>Cen</sup> | Median time to event in<br>days <sup>a</sup><br>[95% CI] <sup>b</sup><br>patients with event<br>n (%) | HR [95% CI] <sup>c</sup><br>p-value <sup>d</sup> |
| Musculoskeletal<br>and connective<br>tissue disorders | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                                | 0.88 [0.05; 14.09]<br>0.9248                     |
| Joint swelling                                        | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                                | NE [NE; NE]<br>0.3237                            |
| Psoriatic<br>arthropathy                              | 242/242                      | NE [NE; NE]<br>0 (0.0)                                                                                | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                                | NE [NE; NE]<br>0.2580                            |
| Nervous system<br>disorders                           | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/236            | NE [NE; NE]<br>4 (1.7)                                                                                | 0.17 [0.02; 1.53]<br>0.0736                      |
| Lethargy                                              | 242/242                      | NE [NE; NE]<br>0 (0.0)                                                                                | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                                | NE [NE; NE]<br>0.2274                            |
| Neuropathy<br>peripheral                              | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                                | 0.98 [0.06; 15.63]<br>0.9903                     |
| Peripheral<br>motor<br>neuropathy                     | 242/242                      | NE [NE; NE]<br>0 (0.0)                                                                                | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                                | NE [NE; NE]<br>0.1573                            |
| Peripheral<br>sensory<br>neuropathy                   | 242/242                      | NE [NE; NE]<br>0 (0.0)                                                                                | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                                | NE [NE; NE]<br>0.1573                            |
| Seizure                                               | 242/242                      | NE [NE; NE]<br>0 (0.0)                                                                                | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                                | NE [NE; NE]<br>0.1573                            |

| Endpoint<br>SOC<br>PT                                    | Lurbinectedin + atezolizumab |                                                                                                       | Atezolizumab       |                                                                                                       | Lurbinectedin + atezolizumab vs.<br>atezolizumab |
|----------------------------------------------------------|------------------------------|-------------------------------------------------------------------------------------------------------|--------------------|-------------------------------------------------------------------------------------------------------|--------------------------------------------------|
|                                                          | N/N <sup>Cen</sup>           | Median time to event in<br>days <sup>a</sup><br>[95% CI] <sup>b</sup><br>patients with event<br>n (%) | N/N <sup>Cen</sup> | Median time to event in<br>days <sup>a</sup><br>[95% CI] <sup>b</sup><br>patients with event<br>n (%) | HR [95% CI] <sup>c</sup><br>p-value <sup>d</sup> |
| Trigeminal<br>neuropathy                                 | 242/242                      | NE [NE; NE]<br>0 (0.0)                                                                                | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                                | NE [NE; NE]<br>0.1573                            |
| Renal and urinary<br>disorders                           | 242/239                      | NE [NE; NE]<br>3 (1.2)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                                | NE [NE; NE]<br>0.1240                            |
| Immune-<br>mediated<br>nephritis                         | 242/240                      | NE [NE; NE]<br>2 (0.8)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                                | NE [NE; NE]<br>0.2392                            |
| Nephropathy                                              | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                                | NE [NE; NE]<br>0.3183                            |
| Respiratory,<br>thoracic and<br>mediastinal<br>disorders | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                                | 0.73 [0.04; 12.05]<br>0.8275                     |
| Dyspnea                                                  | 242/242                      | NE [NE; NE]<br>0 (0.0)                                                                                | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                                | NE [NE; NE]<br>0.1727                            |
| Pneumonitis                                              | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                                | 0.73 [0.04; 12.05]<br>0.8275                     |
| Vascular<br>disorders                                    | 242/240                      | NE [NE; NE]<br>2 (0.8)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                                | NE [NE; NE]<br>0.1643                            |
| Phlebitis                                                | 242/240                      | NE [NE; NE]<br>2 (0.8)                                                                                | 240/240            | N NE [NE; NE]<br>0 (0.0)                                                                              | NE [NE; NE]<br>0.1643                            |

| Endpoint<br>SOC<br>PT                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | Lurbinectedin + atezolizumab |                                                                                                       | Atezolizumab       |                                                                                                       | Lurbinectedin + atezolizumab vs.<br>atezolizumab |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------|-------------------------------------------------------------------------------------------------------|--------------------|-------------------------------------------------------------------------------------------------------|--------------------------------------------------|
|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           | N/N <sup>Cen</sup>           | Median time to event in<br>days <sup>a</sup><br>[95% CI] <sup>b</sup><br>patients with event<br>n (%) | N/N <sup>Cen</sup> | Median time to event in<br>days <sup>a</sup><br>[95% CI] <sup>b</sup><br>patients with event<br>n (%) | HR [95% CI] <sup>c</sup><br>p-value <sup>d</sup> |
| CCOD: 29 July 2024; NE: not estimable.<br>a: summaries of duration (median) are Kaplan-Meier estimates.<br>b: 95% CIs for the median were computed using the method of Brookmeyer and Crowley.<br>c: hazard ratios were estimated using a stratified Cox proportional hazard model. The stratification factors are ECOG PS at randomization (0 vs. 1), LDH at randomization ( $\leq$ ULN vs $>$ ULN) via local laboratory test, presence of liver metastases at enrollment (yes vs. no), and prior receipt of PCI (yes vs. no).<br>d: p-value based on the log rank test. |                              |                                                                                                       |                    |                                                                                                       |                                                  |

Tabelle 8: Subgroup analysis for safety outcomes (IMforte)

| Time point                                               | Lurbinectedin + atezolizumab |                                                                                     |                    | Atezolizumab                                                                        | Lurbinectedin + atezolizumab vs atezolizumab     |
|----------------------------------------------------------|------------------------------|-------------------------------------------------------------------------------------|--------------------|-------------------------------------------------------------------------------------|--------------------------------------------------|
| Outcome <sup>a</sup>                                     | N/N <sup>Cen</sup>           | Median time to event<br>in days <sup>b</sup><br>[95% CI] <sup>c</sup><br>event n () | N/N <sup>Cen</sup> | Median time to<br>event in days <sup>b</sup><br>[95% CI] <sup>c</sup><br>event n () | HR [95% CI] <sup>d</sup><br>p-value <sup>e</sup> |
| Subgroup                                                 |                              |                                                                                     |                    |                                                                                     |                                                  |
| AE of any severity                                       |                              |                                                                                     |                    |                                                                                     |                                                  |
| PCI                                                      |                              |                                                                                     |                    |                                                                                     |                                                  |
| Yes                                                      | 34/0                         | 5.50 [2.00; 10.00]<br>34 (100.0)                                                    | 37/4               | 43.00 [21.00; 81.00]<br>33 (89.2)                                                   | 3.47 [ 1.99; 6.06]<br><.0001                     |
| No                                                       | 208/7                        | 10.00 [9.00; 17.00]<br>201 (96.6)                                                   | 203/42             | 35.00 [24.00; 42.00]<br>161 (79.3)                                                  | 2.07 [ 1.67; 2.56]<br><.0001                     |
| Response to induction                                    |                              |                                                                                     |                    |                                                                                     |                                                  |
| CR                                                       | 7/0                          | 3.00 [2.00; 29.00]<br>7 (100.0)                                                     | 2/1                | NE [12.00; NE]<br>1 (50.0)                                                          | 2.56 [ 0.29; 22.73]<br>0.3794                    |
| PR/SD                                                    | 227/6                        | 10.00 [9.00; 11.00]<br>221 (97.4)                                                   | 235/43             | 35.00 [24.00; 42.00]<br>192 (81.7)                                                  | 2.18 [ 1.78; 2.67]<br><.0001                     |
| SOC blood and lymphatic system disorders                 |                              |                                                                                     |                    |                                                                                     |                                                  |
| Tobacco use history                                      |                              |                                                                                     |                    |                                                                                     |                                                  |
| Current                                                  | 88/58                        | 393.00 [287.00; NE]<br>30 (34.1)                                                    | 72/68              | NE [NE; NE]<br>4 (5.6)                                                              | 7.30 [ 2.56; 20.83]<br><.0001                    |
| Never                                                    | 7/4                          | NE [92.00; NE]<br>3 (42.9)                                                          | 5/3                | NE [22.00; NE]<br>2 (40.0)                                                          | 0.71 [0.12; 4.33]<br>0.7113                      |
| Previous                                                 | 147/79                       | 336.00 [161.00; 400.00]<br>68 (46.3)                                                | 163/147            | NE [NE; NE]<br>16 (9.8)                                                             | 5.38 [ 3.12; 9.26]<br><.0001                     |
| SOC General disorders and administration site conditions |                              |                                                                                     |                    |                                                                                     |                                                  |
| Sex                                                      |                              |                                                                                     |                    |                                                                                     |                                                  |
| Male                                                     | 151/78                       | 263.00 [167.00; 430.00]<br>7 (48.3)                                                 | 150/109            | 610.00 [250.00; NE]<br>41 (27.3)                                                    | 1.86 [1.26; 2.74]<br>0.0015                      |
| Female                                                   | 91/51                        | NE [86.00; NE]<br>40 (44.0)                                                         | 90/67              | NE [NE; NE]<br>23 (25.6)                                                            | 1.99 [ 1.19; 3.33]<br>0.0075                     |

| Time point<br>Outcome <sup>a</sup><br>Subgroup | Lurbinectedin + atezolizumab |                                                                                     | Atezolizumab       |                                                                                     | Lurbinectedin + atezolizumab vs atezolizumab     |
|------------------------------------------------|------------------------------|-------------------------------------------------------------------------------------|--------------------|-------------------------------------------------------------------------------------|--------------------------------------------------|
|                                                | N/N <sup>Cen</sup>           | Median time to event<br>in days <sup>b</sup><br>[95% CI] <sup>c</sup><br>event n () | N/N <sup>Cen</sup> | Median time to event<br>in days <sup>b</sup><br>[95% CI] <sup>c</sup><br>event n () | HR [95% CI] <sup>d</sup><br>p-value <sup>e</sup> |
| Age                                            |                              |                                                                                     |                    |                                                                                     |                                                  |
| <65                                            | 118/63                       | 263.00 [167.00; NE]<br>55 (46.6)                                                    | 90/69              | NE [250.00; NE]<br>21 (23.3)                                                        | 2.21 [ 1.34; 3.66]<br>0.0016                     |
| >=65                                           | 124/66                       | 265.00 [126.00; NE]<br>58 (46.8)                                                    | 150/107            | 610.00 [285.00; NE]<br>43 (28.7)                                                    | 1.83 [ 1.23; 2.73]<br>0.0026                     |
| ECOG PS                                        |                              |                                                                                     |                    |                                                                                     |                                                  |
| 0                                              | 105/56                       | 265.00 [126.00; NE]<br>49 (46.7)                                                    | 102/78             | NE [262.00; NE]<br>24 (23.5)                                                        | 2.21 [ 1.36; 3.62]<br>0.0011                     |
| 1                                              | 137/73                       | 213.00 [129.00; NE]<br>64 (46.7)                                                    | 138/98             | 610.00 [285.00; NE]<br>40 (29.0)                                                    | 1.71 [ 1.15; 2.55]<br>0.0072                     |
| Race                                           |                              |                                                                                     |                    |                                                                                     |                                                  |
| Black or African American                      | 3/1                          | 211.00 [106.00; NE]<br>2 (66.7)                                                     | 1/0                | 18.00 [NE; NE]<br>1 (100.0)                                                         | 0.00 [0.00; NE]<br>0.0833                        |
| Asian                                          | 31/20                        | NE [127.00; NE]<br>11 (35.5)                                                        | 30/26              | NE [NE; NE]<br>4 (13.3)                                                             | 2.68 [ 0.85; 8.48]<br>0.0802                     |
| White                                          | 195/102                      | 263.00 [135.00; 434.00]<br>93 (47.7)                                                | 199/143            | 610.00 [285.00; NE]<br>56 (28.1)                                                    | 1.91 [ 1.36; 2.66]<br>0.0001                     |
| American Indian or Alaska Native               | 1/0                          | 213.00 [NE; NE]<br>1 (100.0)                                                        | 0/0                | NE [NE; NE]<br>NE                                                                   | NE [NE; NE]<br>NE                                |
| LDH                                            |                              |                                                                                     |                    |                                                                                     |                                                  |
| ≤ULN                                           | 176/92                       | 265.00 [167.00; 434.00]<br>84 (47.7)                                                | 179/131            | NE [285.00; NE]<br>48 (26.8)                                                        | 1.880 [ 1.316;<br>2.688]<br>0.0004               |
| >ULN                                           | 66/37                        | 263.00 [115.00; NE]<br>29 (43.9)                                                    | 61/45              | 610.00 [205.00; NE]<br>16 (26.2)                                                    | 2.058 [ 1.101;<br>3.846]<br>0.0208               |

| Time point<br>Outcome <sup>a</sup><br>Subgroup | Lurbinectedin + atezolizumab |                                                                                     | Atezolizumab       |                                                                                  | Lurbinectedin + atezolizumab vs atezolizumab     |
|------------------------------------------------|------------------------------|-------------------------------------------------------------------------------------|--------------------|----------------------------------------------------------------------------------|--------------------------------------------------|
|                                                | N/N <sup>Cen</sup>           | Median time to event<br>in days <sup>b</sup><br>[95% CI] <sup>c</sup><br>event n () | N/N <sup>Cen</sup> | Median time to event in days <sup>b</sup><br>[95% CI] <sup>c</sup><br>event n () | HR [95% CI] <sup>d</sup><br>p-value <sup>e</sup> |
| Liver metastases                               |                              |                                                                                     |                    |                                                                                  |                                                  |
| yes                                            | 100/54                       | 213.00 [115.00; NE]<br>46 (46.0)                                                    | 93/57              | NE [129.00; NE]<br>36 (38.7)                                                     | 1.22 [ 0.79; 1.89]<br>0.3764                     |
| no                                             | 142/75                       | 265.00 [135.00; 434.00]<br>67 (47.2)                                                | 147/119            | 610.00 [NE; NE]<br>28 (19.0)                                                     | 2.76 [ 1.78; 4.29]<br><.0001                     |
| Response to induction                          |                              |                                                                                     |                    |                                                                                  |                                                  |
| CR                                             | 7/3                          | 213.00 [29.00; NE]<br>4 (57.1)                                                      | 2/1                | NE [19.00; NE]<br>1 (50.0)                                                       | 0.58 [ 0.05; 6.49]<br>0.6505                     |
| PR/SD                                          | 227/120                      | 263.00 [167.00; 434.00]<br>107 (47.1)                                               | 235/172            | 610.00 [610.00; NE]<br>63 (26.8)                                                 | 1.93 [ 1.41; 2.65]<br><.0001                     |
| SOC investigations                             |                              |                                                                                     |                    |                                                                                  |                                                  |
| Region                                         |                              |                                                                                     |                    |                                                                                  |                                                  |
| Europe and Middle East                         | 194/128                      | 484.00 [308.00; NE]<br>66 (34.0)                                                    | 190/154            | NE [340.00; NE]<br>36 (18.9)                                                     | 1.78 [1.18; 2.68]<br>0.0052                      |
| North America                                  | 14/11                        | NE [197.00; NE]<br>3 (21.4)                                                         | 17/15              | NE [NE; NE]<br>2 (11.8)                                                          | 1.53 [0.24; 9.62]<br>0.6484                      |
| Central and South America                      | 4/1                          | 36.50 [10.00; NE]<br>3 (75.0)                                                       | 3/1                | 65.00 [42.00; NE]<br>2 (66.7)                                                    | 3.80 [0.38; 37.04]<br>0.2218                     |
| Asia-Pacific                                   | 30/15                        | 198.00 [25.00; NE]<br>15 (50.0)                                                     | 30/22              | 400.00 [NE; NE]<br>8 (26.7)                                                      | 2.34 [0.94; 5.81]<br>0.0611                      |
| SOC psychiatric disorders                      |                              |                                                                                     |                    |                                                                                  |                                                  |
| Tobacco use history                            |                              |                                                                                     |                    |                                                                                  |                                                  |
| Current                                        | 88/81                        | NE [NE; NE]<br>7 (8.0)                                                              | 72/66              | NE [NE; NE]<br>6 (8.3)                                                           | 0.90 [0.30; 2.69]<br>0.850                       |
| Never                                          | 7/6                          | NE [198.00; NE]<br>1 (14.3)                                                         | 5/5                | NE [NE; NE]<br>0 (0.0)                                                           | NE [0.00; NE]<br>0.6547                          |

| Time point<br>Outcome <sup>a</sup><br>Subgroup | Lurbinectedin + atezolizumab |                                                                                     | Atezolizumab       |                                                                                     | Lurbinectedin + atezolizumab vs atezolizumab     |
|------------------------------------------------|------------------------------|-------------------------------------------------------------------------------------|--------------------|-------------------------------------------------------------------------------------|--------------------------------------------------|
|                                                | N/N <sup>Cen</sup>           | Median time to event<br>in days <sup>b</sup><br>[95% CI] <sup>c</sup><br>event n () | N/N <sup>Cen</sup> | Median time to event<br>in days <sup>b</sup><br>[95% CI] <sup>c</sup><br>event n () | HR [95% CI] <sup>d</sup><br>p-value <sup>e</sup> |
| Previous                                       | 147/133                      | NE [NE; NE]<br>14 (9.5)                                                             | 163/161            | NE [NE; NE]<br>2 (1.2)                                                              | 6.54 [1.48; 28.57]<br>0.0043                     |
| Severe AE (CTCAE ≥3) <sup>g</sup>              |                              |                                                                                     |                    |                                                                                     |                                                  |
| PCI                                            |                              |                                                                                     |                    |                                                                                     |                                                  |
| Yes                                            | 34/15                        | 280.00 [39.00; 349.00]<br>19 (55.9)                                                 | 37/24              | NE [205.00; NE]<br>13 (35.1)                                                        | 1.84 [ 0.91; 3.73]<br>0.0865                     |
| No                                             | 208/123                      | 343.00 [223.00; NE]<br>85 (40.9)                                                    | 203/157            | NE [326.00; NE]<br>46 (22.7)                                                        | 1.74 [ 1.21; 2.51]<br>0.0023                     |
| Response to induction                          |                              |                                                                                     |                    |                                                                                     |                                                  |
| CR                                             | 7/3                          | 147.00 [11.00; NE]<br>4 (57.1)                                                      | 2/2                | NE [NE; NE]<br>0 (0.0)                                                              | NE [0.00; NE]<br>0.2604                          |
| PR/SD                                          | 227/127                      | 336.00 [223.00; 393.00]<br>100 (44.1)                                               | 235/176            | NE [326.00; NE]<br>59 (25.1)                                                        | 1.75 [ 1.27; 2.43]<br>0.0006                     |
| Grade 3 AE                                     |                              |                                                                                     |                    |                                                                                     |                                                  |
| PCI                                            |                              |                                                                                     |                    |                                                                                     |                                                  |
| Yes                                            | 34/18                        | 343.00 [43.00; NE]<br>16 (47.1)                                                     | 37/27              | NE [218.00; NE]<br>10 (27.0)                                                        | 2.00 [ 0.91; 4.43]<br>0.0799                     |
| No                                             | 208/129                      | 393.00 [343.00; NE]<br>79 (38.0)                                                    | 203/166            | NE [NE; NE]<br>37 (18.2)                                                            | 2.03 [ 1.37; 3.01]<br>0.0003                     |
| Response to Induction                          |                              |                                                                                     |                    |                                                                                     |                                                  |
| CR                                             | 7/4                          | NE [30.00; NE]<br>3 (42.9)                                                          | 2/2                | NE [NE; NE]<br>0 (0.0)                                                              | NE [0.00; NE]<br>0.3340                          |
| PR/SD                                          | 227/135                      | 349.00 [336.00; 405.00]<br>92 (40.5)                                                | 235/188            | NE [NE; NE]<br>47 (20.0)                                                            | 2.04 [ 1.43; 2.90]<br><.0001                     |
| Grade 4 AE                                     |                              |                                                                                     |                    |                                                                                     |                                                  |

| Time point<br>Outcome <sup>a</sup><br>Subgroup | Lurbinectedin + atezolizumab |                                                                                     | Atezolizumab       |                                                                                  | Lurbinectedin + atezolizumab vs atezolizumab     |
|------------------------------------------------|------------------------------|-------------------------------------------------------------------------------------|--------------------|----------------------------------------------------------------------------------|--------------------------------------------------|
|                                                | N/N <sup>Cen</sup>           | Median time to event<br>in days <sup>b</sup><br>[95% CI] <sup>c</sup><br>event n () | N/N <sup>Cen</sup> | Median time to event in days <sup>b</sup><br>[95% CI] <sup>c</sup><br>event n () | HR [95% CI] <sup>d</sup><br>p-value <sup>e</sup> |
| PCI                                            |                              |                                                                                     |                    |                                                                                  |                                                  |
| Yes                                            | 34/27                        | NE [NE; NE]<br>7 (20.6)                                                             | 37/35              | NE [NE; NE]<br>2 (5.4)                                                           | 3.91 [ 0.81; 18.87]<br>0.0679                    |
| No                                             | 208/188                      | NE [484.00; NE]<br>20 (9.6)                                                         | 203/195            | NE [NE; NE]<br>8 (3.9)                                                           | 2.22 [ 0.98; 5.08]<br>0.0514                     |
| Response to Induction                          |                              |                                                                                     |                    |                                                                                  |                                                  |
| CR                                             | 7/6                          | NE [NE; NE]<br>1 (14.3)                                                             | 2/2                | NE [NE; NE]<br>0 (0.0)                                                           | NE [0.00; NE]<br>0.5637                          |
| PR/SD                                          | 227/201                      | NE [484.00; NE]<br>26 (11.5)                                                        | 235/225            | NE [NE; NE]<br>10 (4.3)                                                          | 2.55 [ 1.23; 5.32]<br>0.0094                     |
| Grade 5 AE                                     |                              |                                                                                     |                    |                                                                                  |                                                  |
| PCI                                            |                              |                                                                                     |                    |                                                                                  |                                                  |
| Yes                                            | 34/32                        | NE [NE; NE]<br>2 (5.9)                                                              | 37/36              | NE [NE; NE]<br>1 (2.7)                                                           | 1.97 [ 0.18; 21.74]<br>0.5743                    |
| No                                             | 208/198                      | NE [NE; NE]<br>10 (4.8)                                                             | 203/198            | NE [NE; NE]<br>5 (2.5)                                                           | 1.57 [ 0.53; 4.63]<br>0.4147                     |
| Response to Induction                          |                              |                                                                                     |                    |                                                                                  |                                                  |
| CR                                             | 7/6                          | NE [NE; NE]<br>1 (14.3)                                                             | 2/2                | NE [NE; NE]<br>0 (0.0)                                                           | NE [0.00; NE]<br>0.5930                          |
| PR/SD                                          | 227/216                      | NE [NE; NE]<br>11 (4.8)                                                             | 235/229            | NE [NE; NE]<br>6 (2.6)                                                           | 1.58 [ 0.58; 4.29]<br>0.3693                     |
| Serious AE                                     |                              |                                                                                     |                    |                                                                                  |                                                  |
| PCI                                            |                              |                                                                                     |                    |                                                                                  |                                                  |
| Yes                                            | 34/18                        | 287.00 [41.00; NE]<br>16 (47.1)                                                     | 37/25              | NE [218.00; NE]<br>12 (32.4)                                                     | 1.63 [ 0.77; 3.45]<br>0.2007                     |

| Time point<br>Outcome <sup>a</sup><br>Subgroup | Lurbinectedin + atezolizumab |                                                                                     | Atezolizumab       |                                                                                     | Lurbinectedin + atezolizumab vs atezolizumab     |
|------------------------------------------------|------------------------------|-------------------------------------------------------------------------------------|--------------------|-------------------------------------------------------------------------------------|--------------------------------------------------|
|                                                | N/N <sup>Cen</sup>           | Median time to event<br>in days <sup>b</sup><br>[95% CI] <sup>c</sup><br>event n () | N/N <sup>Cen</sup> | Median time to event<br>in days <sup>b</sup><br>[95% CI] <sup>c</sup><br>event n () | HR [95% CI] <sup>d</sup><br>p-value <sup>e</sup> |
| No                                             | 208/149                      | NE [NE; NE]<br>59 (28.4)                                                            | 203/174            | NE [NE; NE]<br>29 (14.3)                                                            | 1.8 [ 1.15; 2.82]<br>0.0092                      |
| Response to Induction                          |                              |                                                                                     |                    |                                                                                     |                                                  |
| CR                                             | 7/6                          | NE [NE; NE]<br>1 (14.3)                                                             | 2/2                | NE [NE; NE]<br>0 (0.0)                                                              | NE [0.00; NE]<br>0.5930                          |
| PR/SD                                          | 227/154                      | NE [358.00; NE]<br>73 (32.2)                                                        | 235/194            | NE [NE; NE]<br>41 (17.4)                                                            | 1.75 [ 1.19; 2.56]<br>0.0040                     |
| AE leading to treatment discontinuation        |                              |                                                                                     |                    |                                                                                     |                                                  |
| PCI                                            |                              |                                                                                     |                    |                                                                                     |                                                  |
| Yes                                            | 34/30                        | NE [393.00; NE]<br>4 (11.8)                                                         | 37/32              | NE [269.00; NE]<br>5 (13.5)                                                         | 0.73 [ 0.19; 2.75]<br>0.6363                     |
| No                                             | 208/197                      | NE [NE; NE]<br>11 (5.3)                                                             | 203/200            | NE [NE; NE]<br>3 (1.5)                                                              | 3.33 [ 0.93; 12.05]<br>0.0502                    |
| Response to Induction                          |                              |                                                                                     |                    |                                                                                     |                                                  |
| CR                                             | 7/7                          | NE [NE; NE]<br>0 (0.0)                                                              | 2/2                | NE [NE; NE]<br>0 (0.0)                                                              | NE [NE; NE]<br>NE                                |
| PR/SD                                          | 227/212                      | NE [NE; NE]<br>15 (6.6)                                                             | 235/227            | NE [NE; NE]<br>8 (3.4)                                                              | 1.71 [ 0.72; 4.05]<br>0.2195                     |
| Immune-related AE <sup>h</sup>                 |                              |                                                                                     |                    |                                                                                     |                                                  |
| PCI                                            |                              |                                                                                     |                    |                                                                                     |                                                  |
| Yes                                            | 34/26                        | NE [NE; NE]<br>8 (23.5)                                                             | 37/26              | NE [253.000; NE]<br>11 (29.7)                                                       | 0.81 [ 0.32; 2.01]<br>0.6421                     |
| No                                             | 208/141                      | 444.000 [316.000; NE]<br>67 (32.2)                                                  | 203/160            | NE [NE; NE]<br>43 (21.2)                                                            | 1.37 [ 0.93; 2.02]<br>0.1099                     |
| Response to Induction                          |                              |                                                                                     |                    |                                                                                     |                                                  |

| Time point<br>Outcome <sup>a</sup><br>Subgroup                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  | Lurbinectedin + atezolizumab |                                                                                     | Atezolizumab       |                                                                                     | Lurbinectedin + atezolizumab vs atezolizumab     |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------|-------------------------------------------------------------------------------------|--------------------|-------------------------------------------------------------------------------------|--------------------------------------------------|
|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 | N/N <sup>Cen</sup>           | Median time to event<br>in days <sup>b</sup><br>[95% CI] <sup>c</sup><br>event n () | N/N <sup>Cen</sup> | Median time to event<br>in days <sup>b</sup><br>[95% CI] <sup>c</sup><br>event n () | HR [95% CI] <sup>d</sup><br>p-value <sup>e</sup> |
| CR                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              | 7/4                          | NE [23.000; NE]<br>3 (42.9)                                                         | 2/1                | NE [41.000; NE]<br>1 (50.0)                                                         | 1.06 [ 0.11; 10.31]<br>0.9622                    |
| PR/SD                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           | 227/156                      | 444.000 [324.000; NE]<br>71 (31.3)                                                  | 235/182            | NE [NE; NE]<br>53 (22.6)                                                            | 1.27 [ 0.89; 1.83]<br>0.1862                     |
| <p>Reading the “Hypothesis testing” columns:</p> <p>1. Statistical significance: S = Statistically significant against the alpha level specified in the statistical analysis plan of the corresponding study, NS = Non-significant, NO = Nominal p-value</p> <p>2. Prespecification: P = Statistical test was prespecified according to the statistical analysis plan of the corresponding study, NP = Not prespecified</p> <p>3. Multiple hypothesis testing. C = Appropriate control for multiplicity according to the statistical analysis plan and clinical study report of the corresponding study, NC = Not controlled</p> <p>CCOD: 29 July 2024; NE: not estimable.</p> <p>a: for AE according to SOC and PT only subgroups with a statistically significant interaction p-value are presented.</p> <p>b: summaries of duration (median) are Kaplan-Meier estimates.</p> <p>c: 95% CIs for the median were computed using the method of Brookmeyer and Crowley.</p> <p>d: hazard ratios were estimated using a Cox proportional hazard model. The stratification factors are ECOG PS at randomization (0 vs. 1), LDH at randomization (<math>\leq</math>ULN vs <math>&gt;</math>ULN) via local laboratory test, presence of liver metastases at enrollment (yes vs. no), and prior receipt of PCI (yes vs. no).</p> <p>e: p-value based on the log rank test.</p> <p>f: quantile regression analysis.</p> <p>g: if a patient experienced either repeated occurrences of the same adverse event or two different adverse events, one Grade 3 and one Grade 4, they are counted only once in the Grade <math>\geq 3</math> category.</p> <p>h: specific AE, as requested by the assessment scope. Immune-related AE were calculated as a combined endpoint comprising the following immune-mediated AE: adrenal insufficiency, colitis, diabetes mellitus, encephalitis, Guillain-Barre syndrome, hepatitis (diagnosis and lab abnormalities), hepatitis (diagnosis), hepatitis (lab abnormalities), hyperthyroidism, hypothyroidism, meningoencephalitis, myositis, myositis (myositis + rhabdomyolysis) nephritis, ocular inflammatory toxicity, pancreatitis, pericardial disorders, pneumonitis, rhabdomyolysis, rash, severe cutaneous reactions, and vasculitis.</p> |                              |                                                                                     |                    |                                                                                     |                                                  |

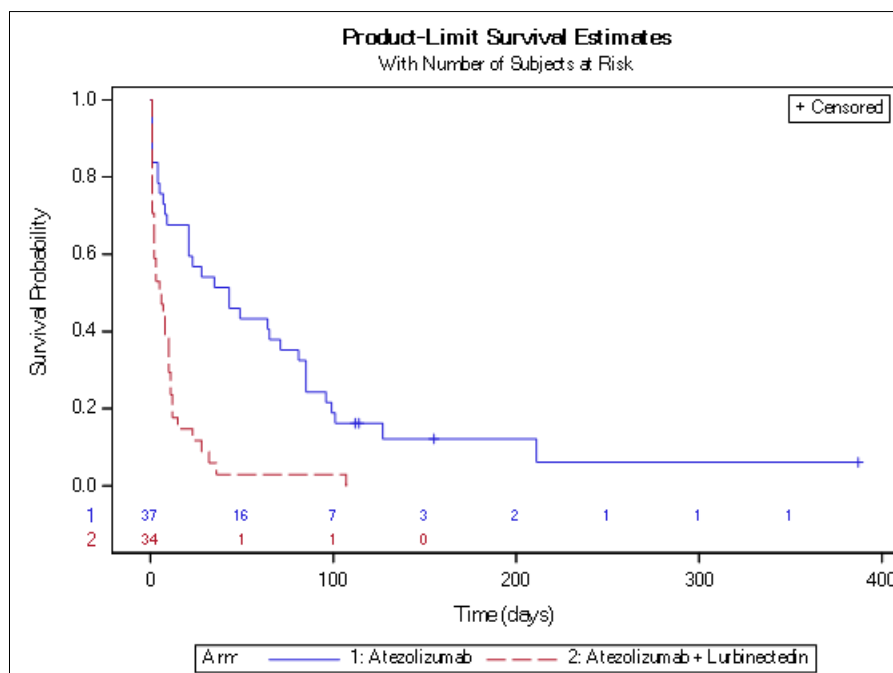


Abbildung 49: Kaplan-Meier plot for any AE, patients receiving PCI prior to randomization, IMforte trial, Safety Analysis Set, CCOD 29 July 2024

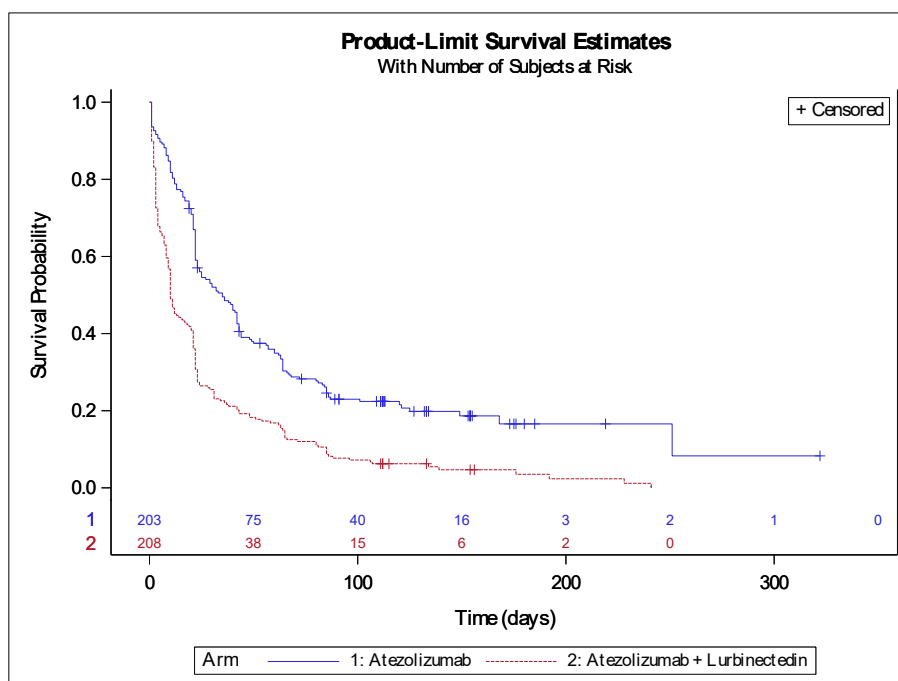


Abbildung 50: Kaplan-Meier plot for any AE, patients not receiving PCI prior to randomization, IMforte trial, Safety Analysis Set, CCOD 29 July 2024

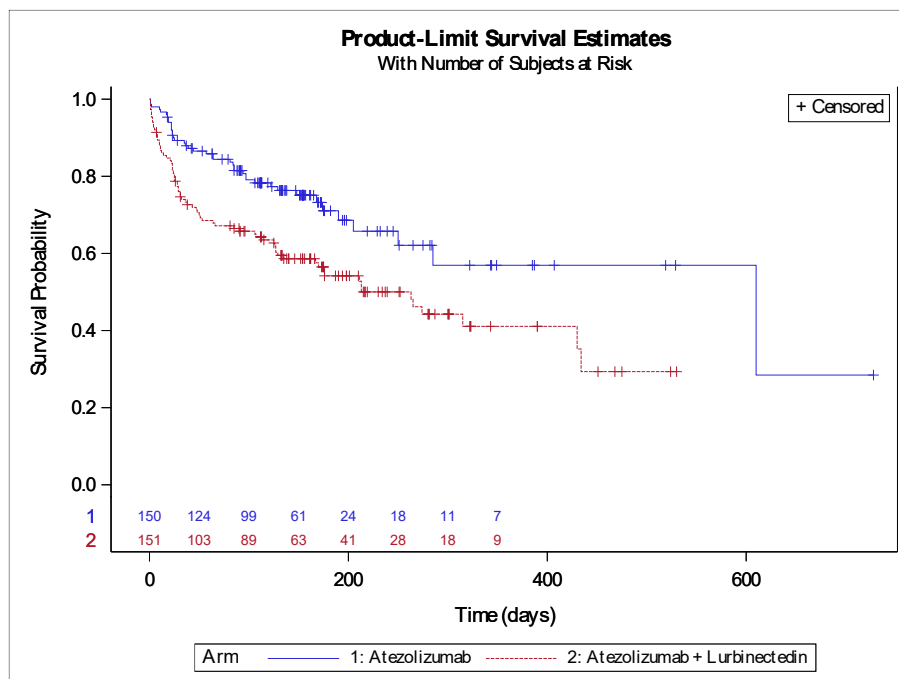


Abbildung 51: Kaplan-Meier plot for any AE (SOC general disorders and administration site conditions), male patients, IMforte trial, Safety Analysis Set, CCOD 29 July 2024

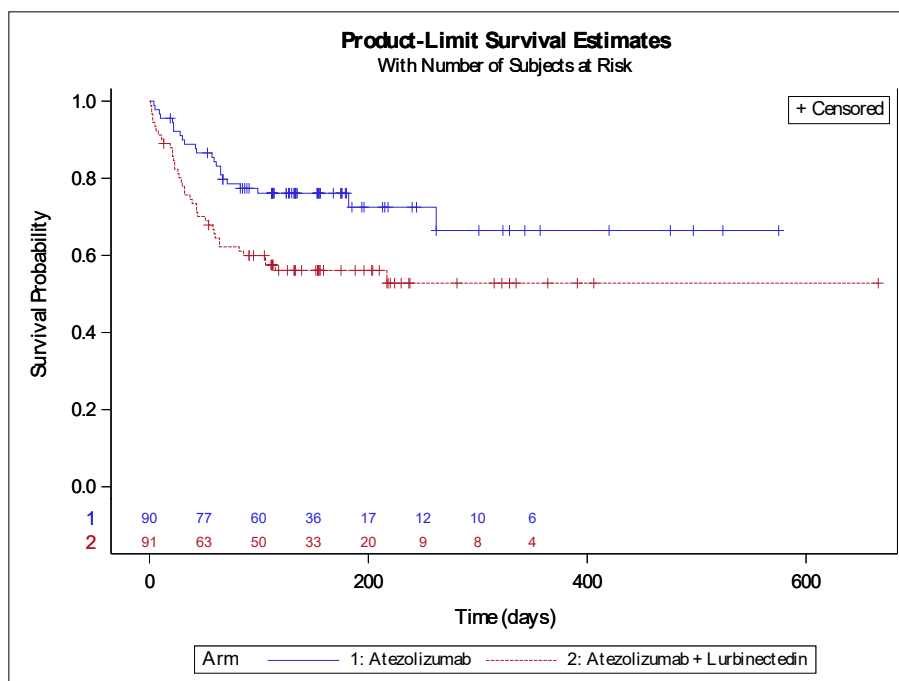


Abbildung 52: Kaplan-Meier plot for any AE (SOC general disorders and administration site conditions), female patients, IMforte trial, Safety Analysis Set, CCOD 29 July 2024

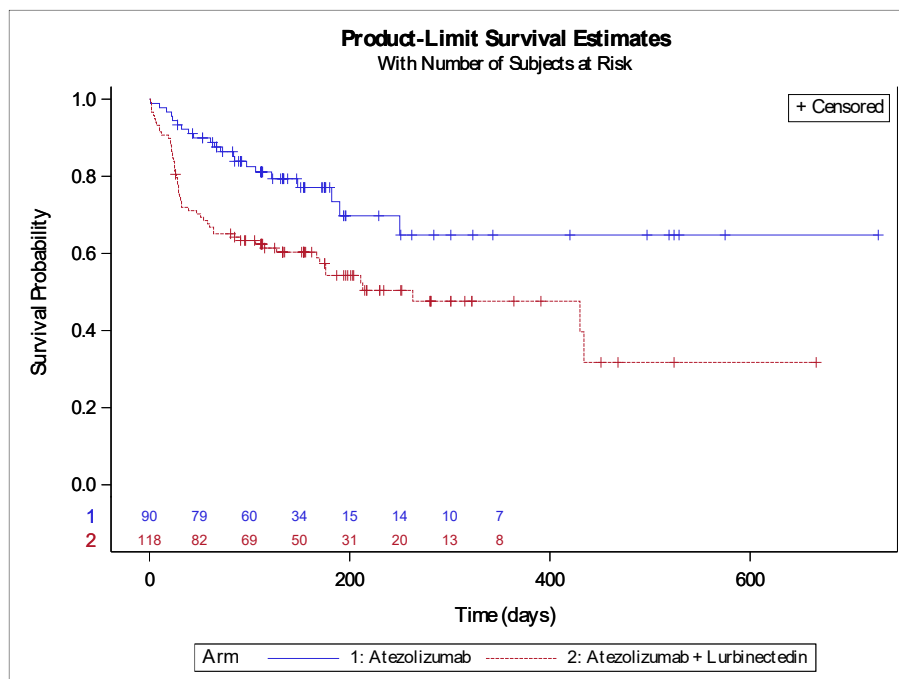


Abbildung 53: Kaplan-Meier plot for any AE (SOC general disorders and administration site conditions), patients aged <65 years, IMforte trial, Safety Analysis Set, CCOD 29 July 2024

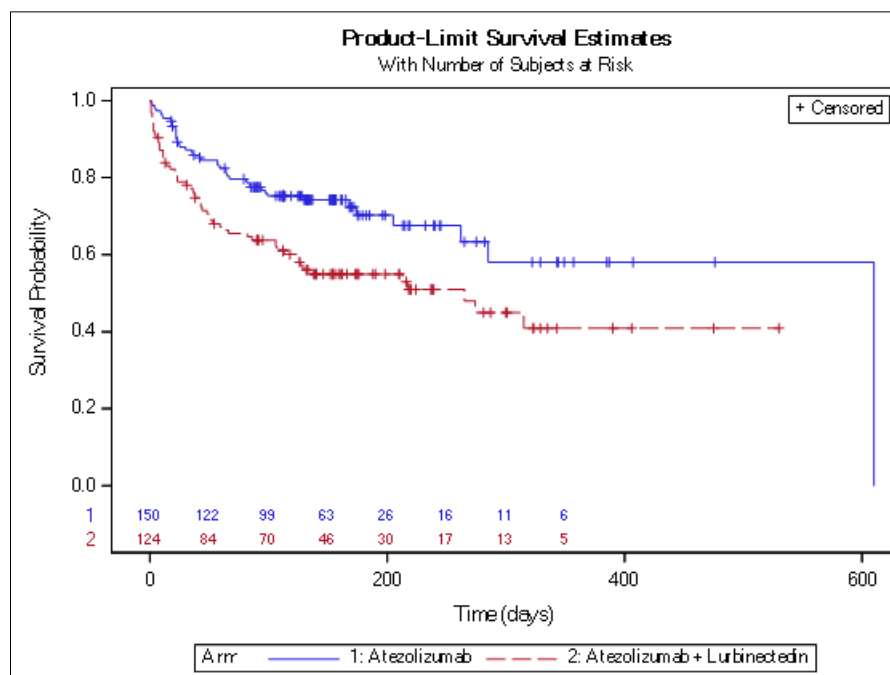


Abbildung 54: Kaplan-Meier plot for any AE (SOC general disorders and administration site conditions), patients aged ≥65 years, IMforte trial, Safety Analysis Set, CCOD 29 July 2024

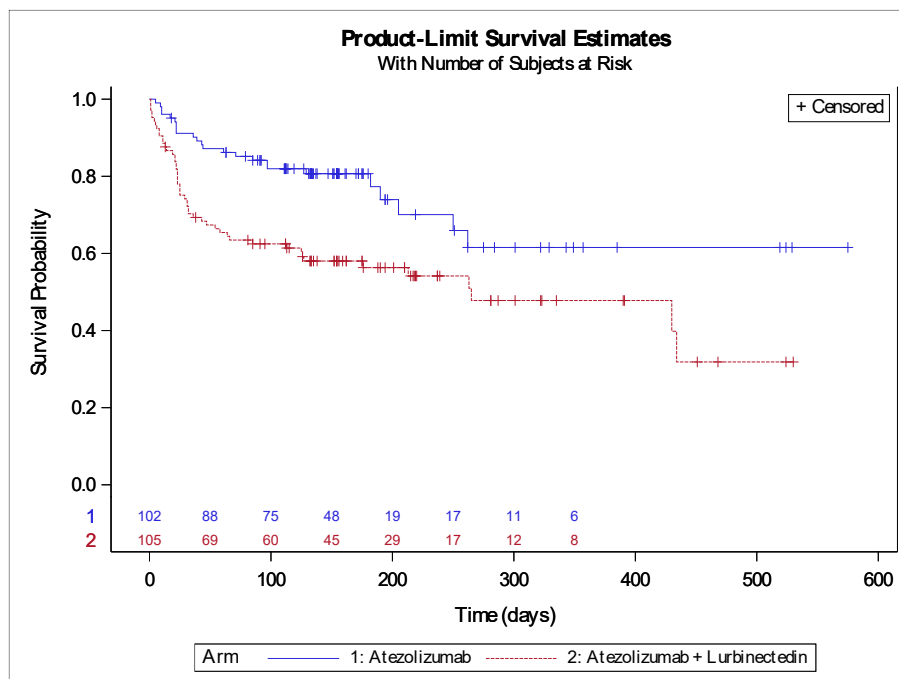


Abbildung 55: Kaplan-Meier plot for any AE (SOC general disorders and administration site conditions), patients with ECOG PS 0, IMforte trial, Safety Analysis Set, CCOD 29 July 2024

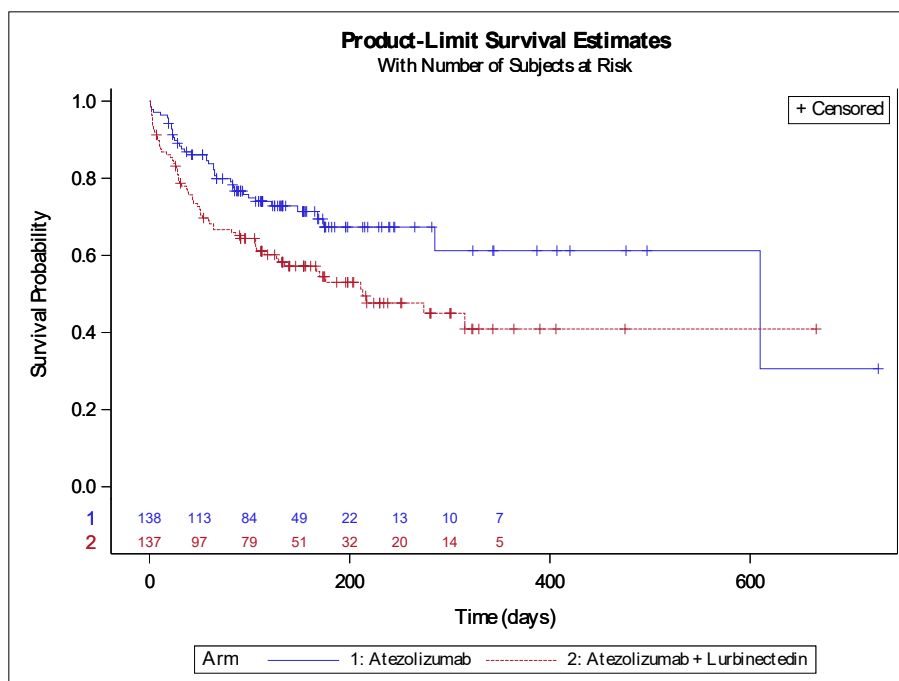


Abbildung 56: Kaplan-Meier plot for any AE (SOC general disorders and administration site conditions), patients with ECOG PS 1, IMforte trial, Safety Analysis Set, CCOD 29 July 2024

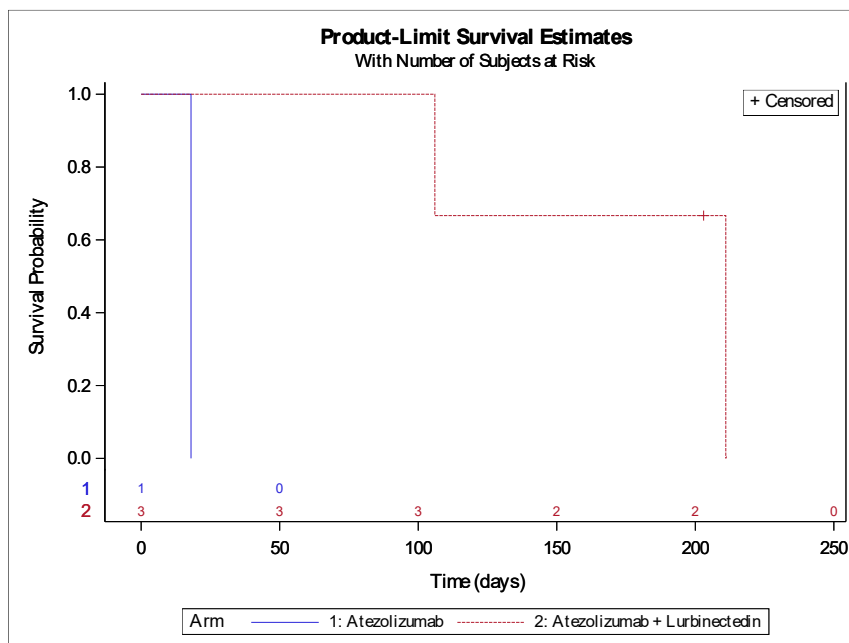


Abbildung 57: Kaplan-Meier plot for any AE (SOC general disorders and administration site conditions), patients of Black or African American race, IMforte trial, Safety Analysis Set, CCOD 29 July 2024

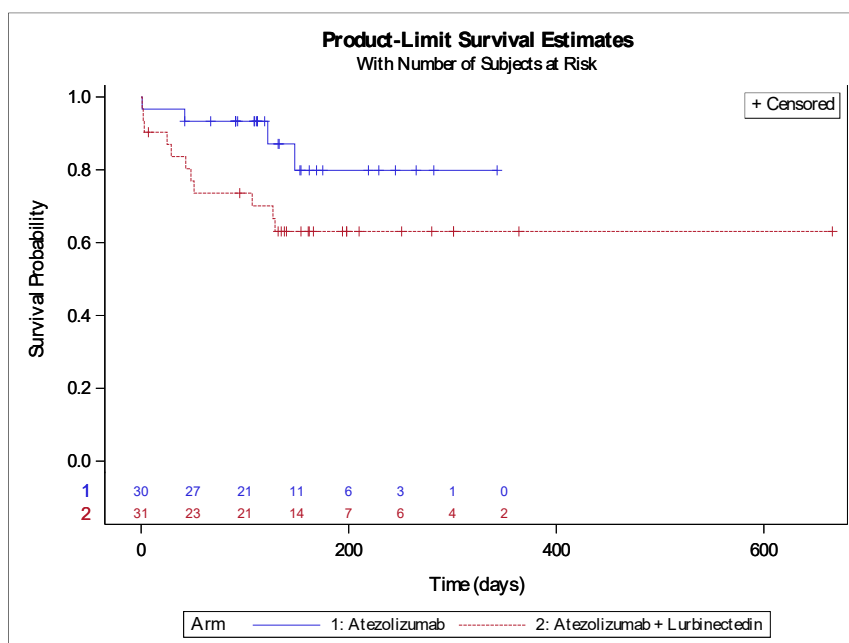


Abbildung 58: Kaplan-Meier plot for any AE (SOC general disorders and administration site conditions), patients of Asian race, IMforte trial, Safety Analysis Set, CCOD 29 July 2024

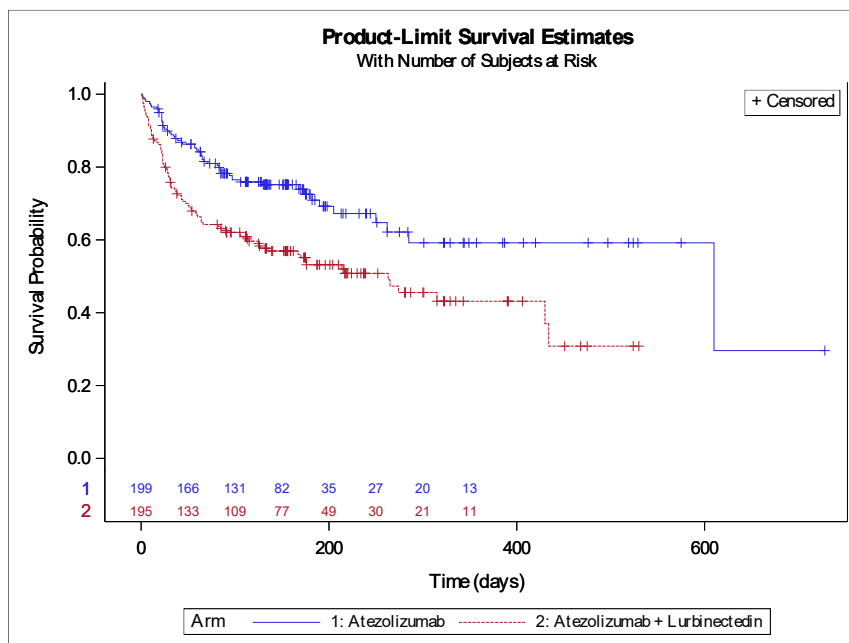


Figure 1: Kaplan-Meier plot for any AE (SOC general disorders and administration site conditions), patients of White race, IMforte trial, Safety Analysis Set, CCOD 29 July 2024

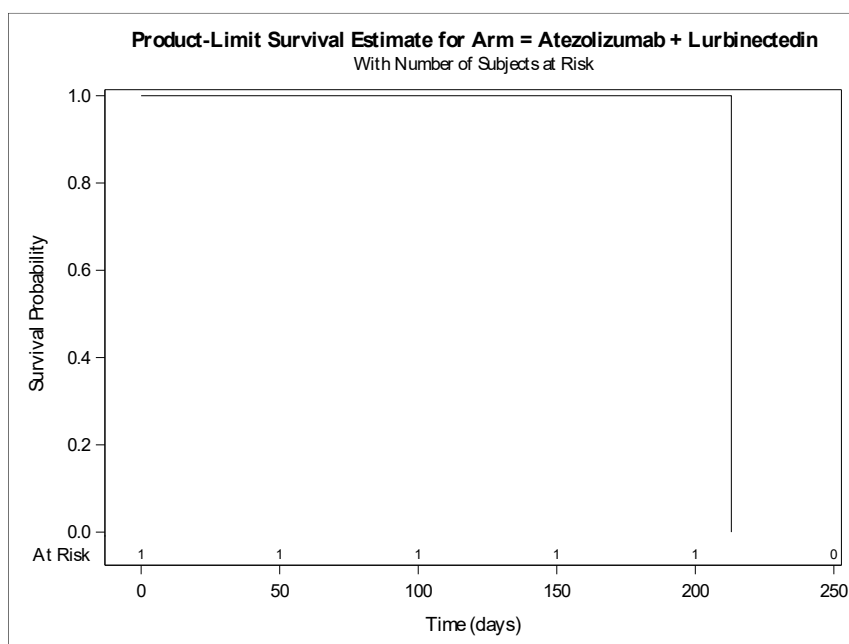


Abbildung 59: Kaplan-Meier plot for any AE (SOC general disorders and administration site conditions), patients of American Indian or Alaska Native race, IMforte trial, Safety Analysis Set, CCOD 29 July 2024

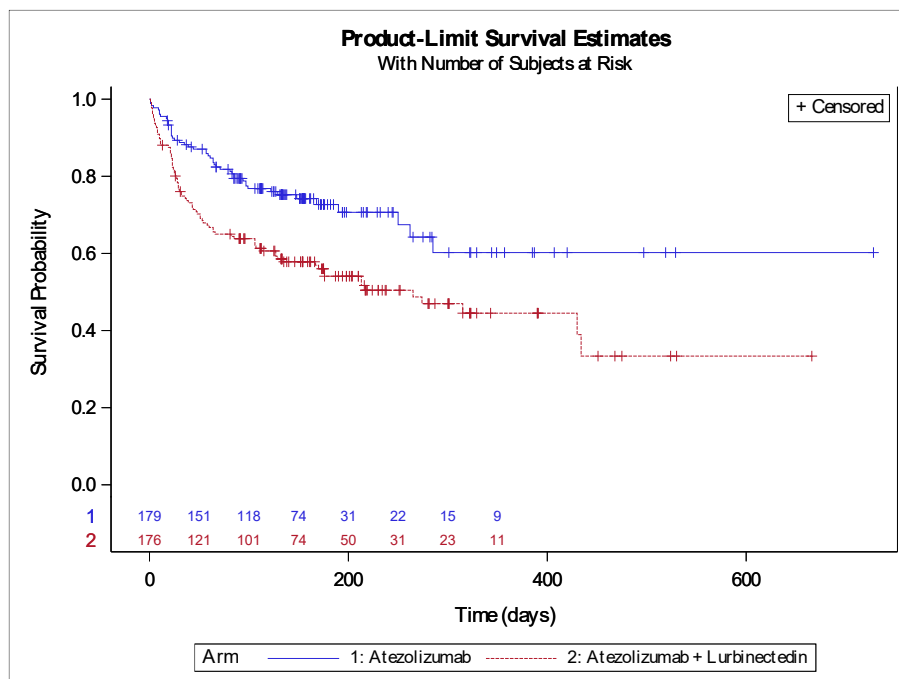


Abbildung 60: Kaplan-Meier plot for any AE (SOC general disorders and administration site conditions), patients with LDH  $\leq$ ULN, IMforte trial, Safety Analysis Set, CCOD 29 July 2024

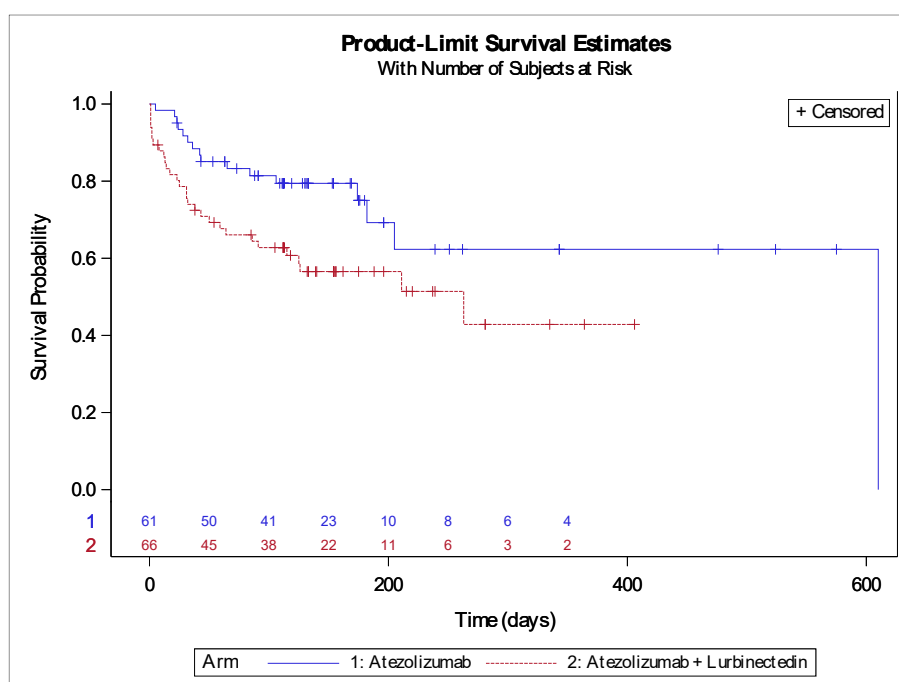


Abbildung 61: Kaplan-Meier plot for any AE (SOC general disorders and administration site conditions), patients with LDH >ULN, IMforte trial, Safety Analysis Set, CCOD 29 July 2024

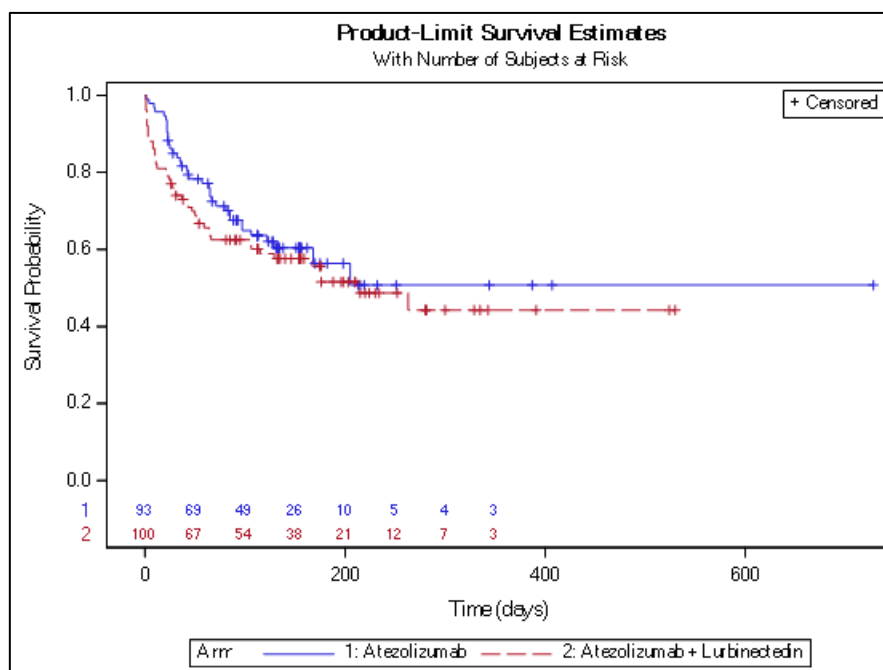


Abbildung 62: Kaplan-Meier plot for any AE (SOC general disorders and administration site conditions), patients with liver metastases at induction treatment, IMforte trial, Safety Analysis Set, CCOD 29 July 2024

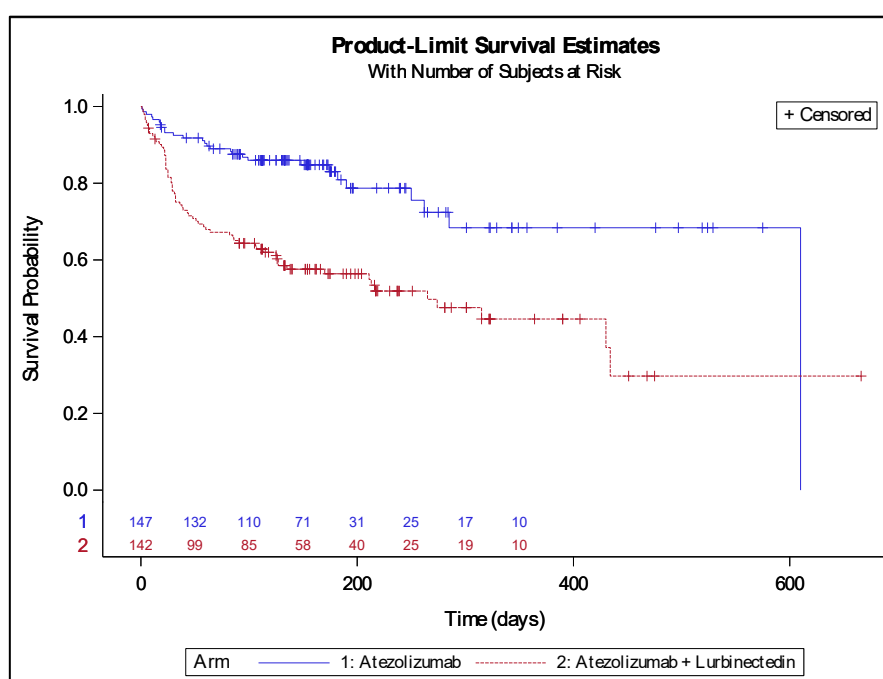


Abbildung 63: Kaplan-Meier plot for any AE (SOC general disorders and administration site conditions), patients without liver metastases at induction treatment, IMforte trial, Safety Analysis Set, CCOD 29 July 2024

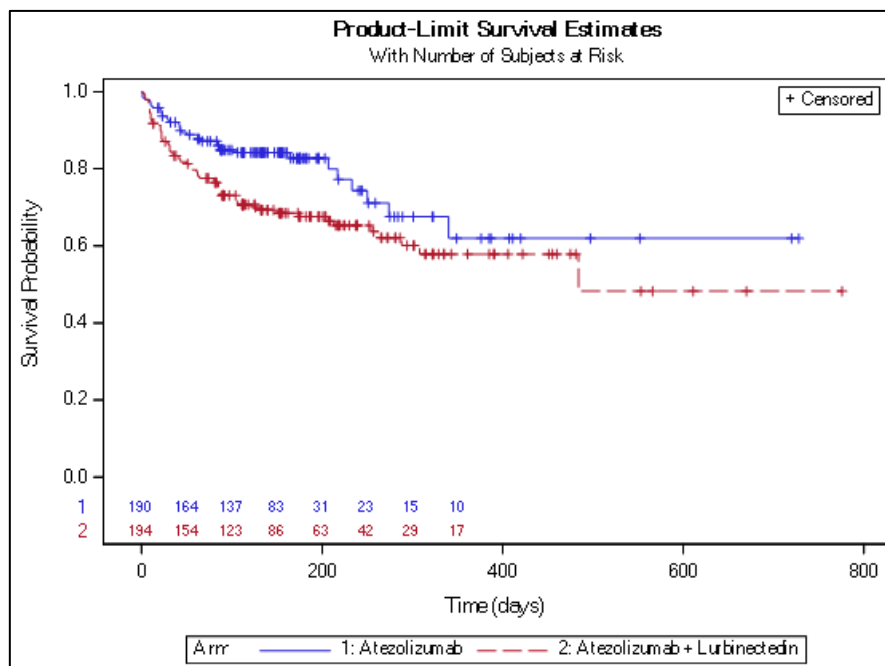


Abbildung 64: Kaplan-Meier plot for any AE, (SOC investigations), patients from Europe and Middle East, IMforte trial, Safety Analysis Set, CCOD 29 July 2024

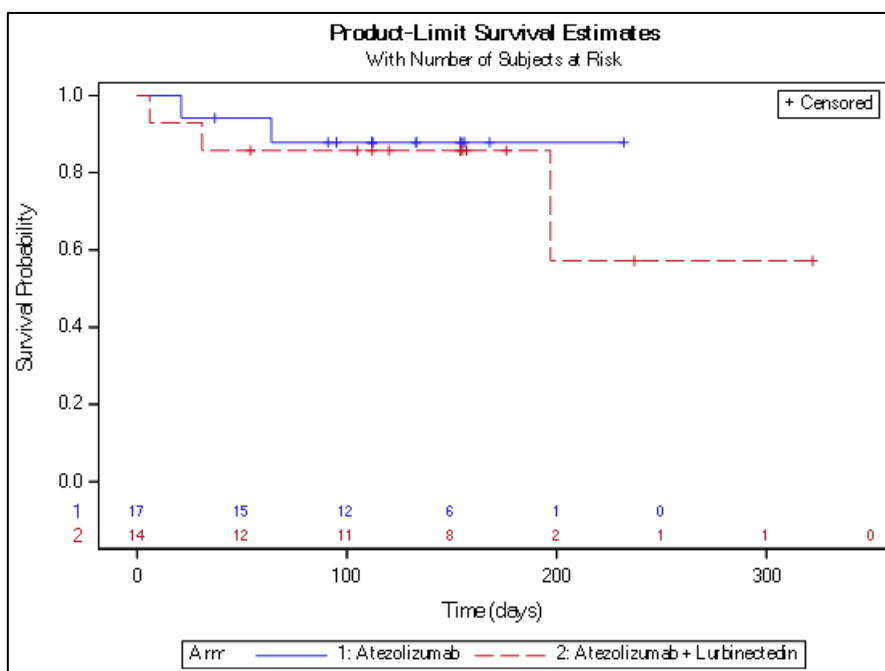


Abbildung 65: Kaplan-Meier plot for any AE, (SOC investigations), patients from North America, IMforte trial, Safety Analysis Set, CCOD 29 July 2024

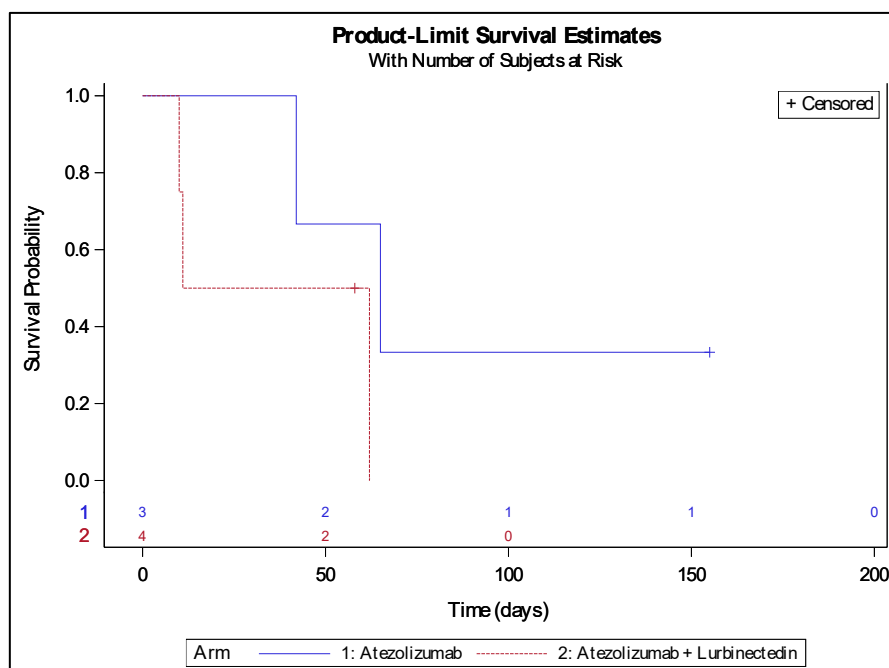


Abbildung 66: Kaplan-Meier plot for any AE, (SOC investigations), patients from Central and South America, IMforte trial, Safety Analysis Set, CCOD 29 July 2024

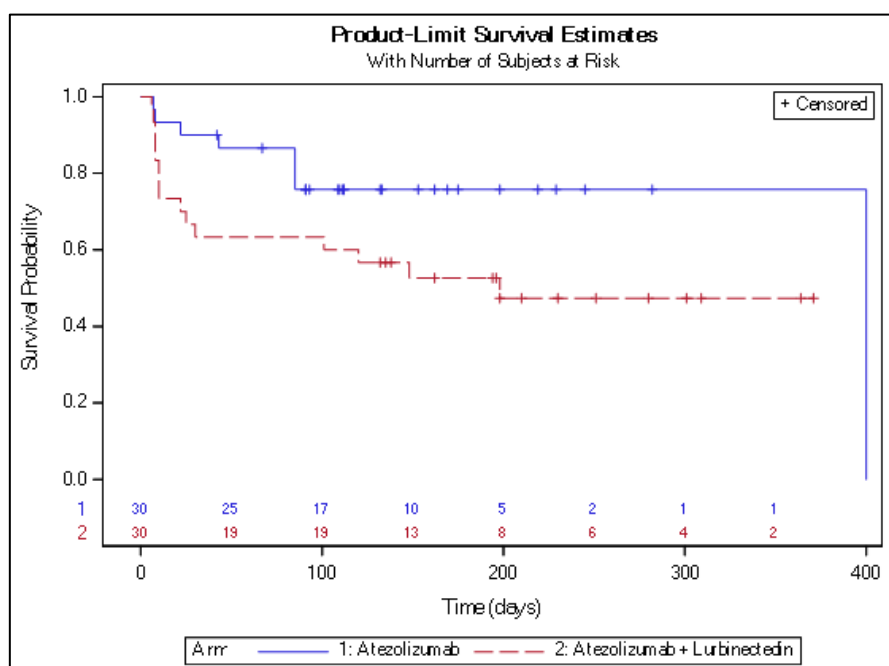


Abbildung 67: Kaplan-Meier plot for any AE, (SOC investigations), patients from Asia-Pacific, IMforte trial, Safety Analysis Set, CCOD 29 July 2024

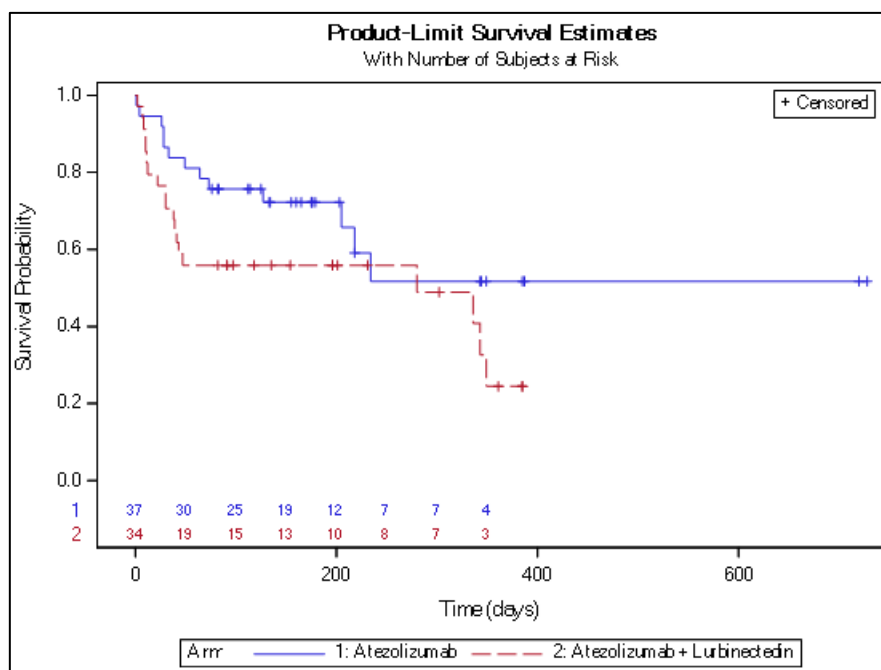


Abbildung 68: Kaplan-Meier plot for severe AE (grade  $\geq 3$ ), patients receiving PCI prior to randomization, IMforte trial, Safety Analysis Set, CCOD 29 July 2024

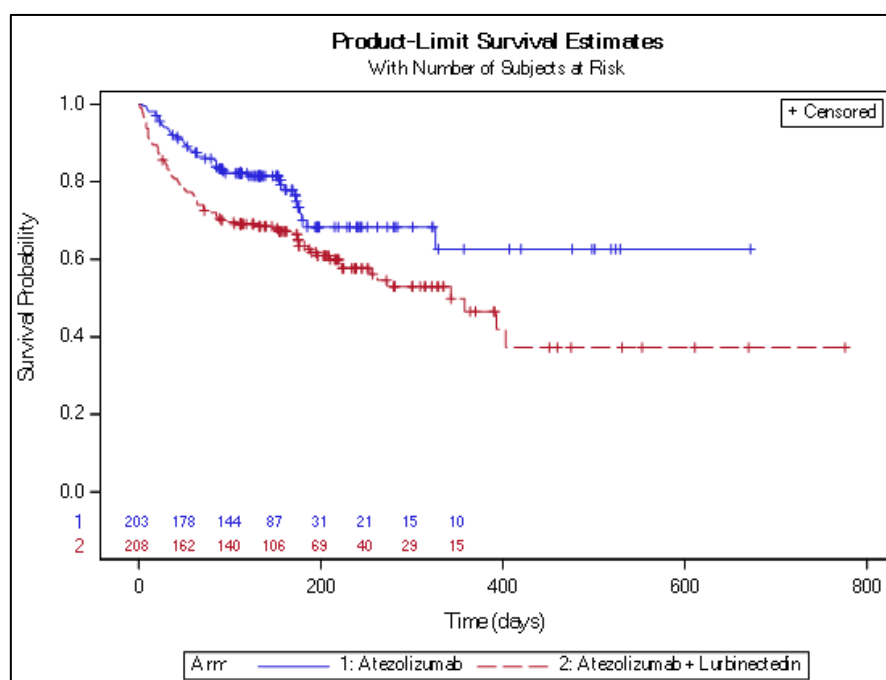


Abbildung 69: Kaplan-Meier plot for severe AE (grade  $\geq 3$ ), patients not receiving PCI prior to randomization, IMforte trial, Safety Analysis Set, CCOD 29 July 2024

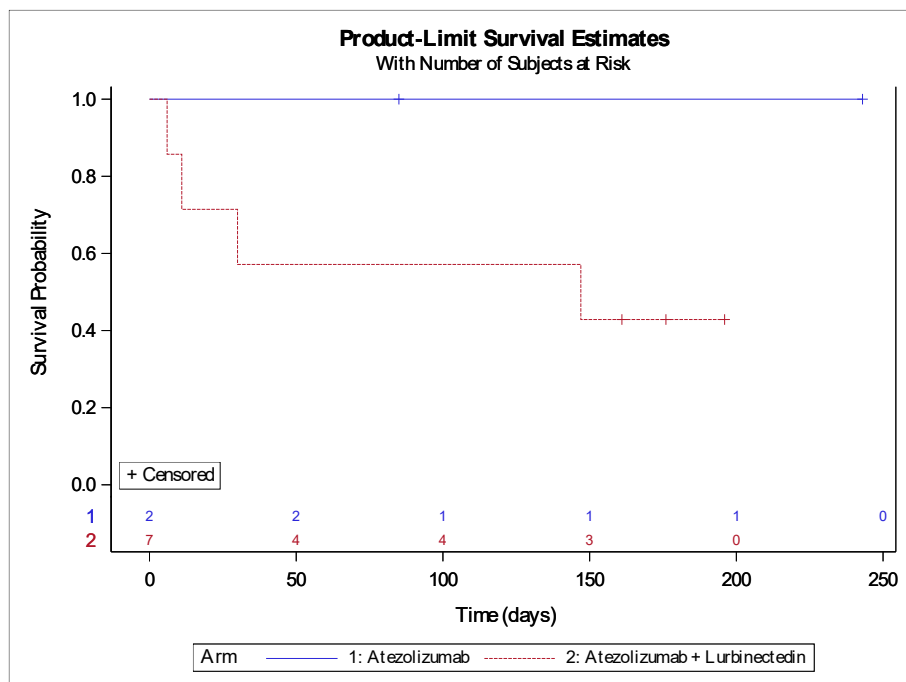


Abbildung 70: Kaplan-Meier plot for severe AE (grade  $\geq 3$ ), patients with CR to induction treatment, IMforte trial, Safety Analysis Set, CCOD 29 July 2024

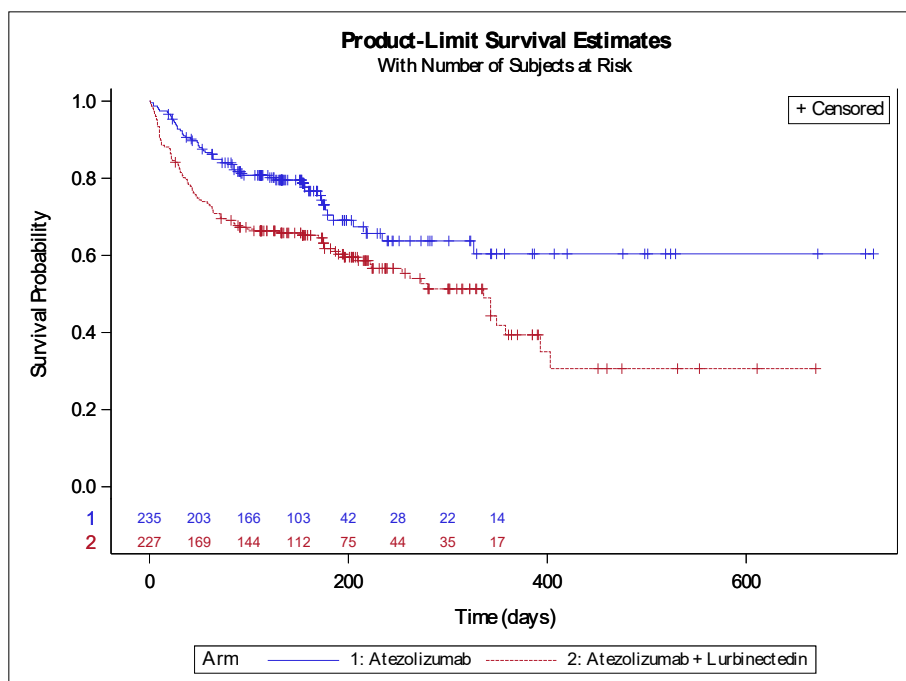


Abbildung 71: Kaplan-Meier plot for severe AE (grade  $\geq 3$ ), patients with PR/SD to induction treatment, IMforte trial, Safety Analysis Set, CCOD 29 July 2024

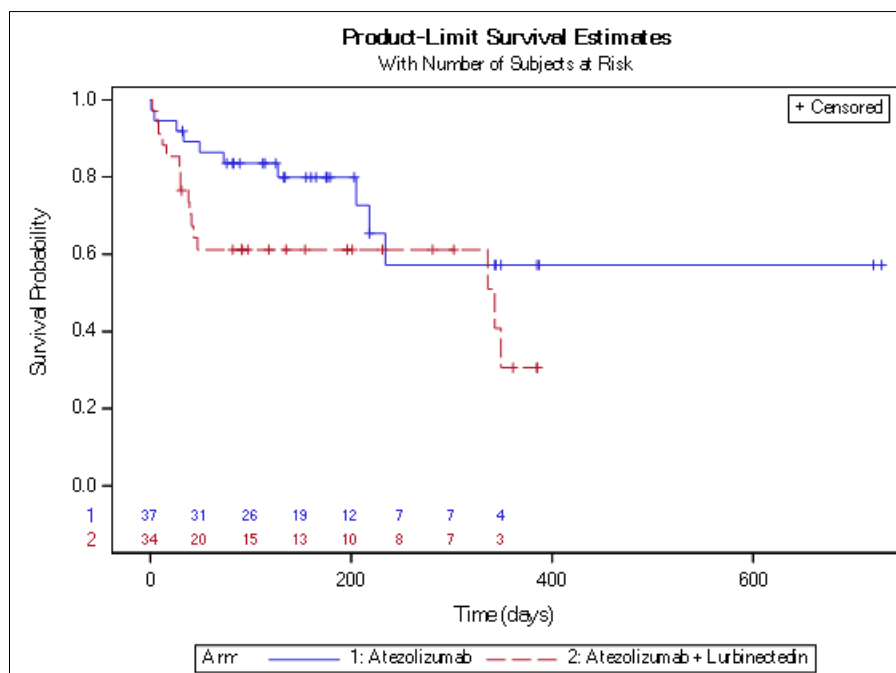


Abbildung 72: Kaplan-Meier plot for AE grade 3, patients receiving PCI prior to randomization, IMforte trial, Safety Analysis Set, CCOD 29 July 2024

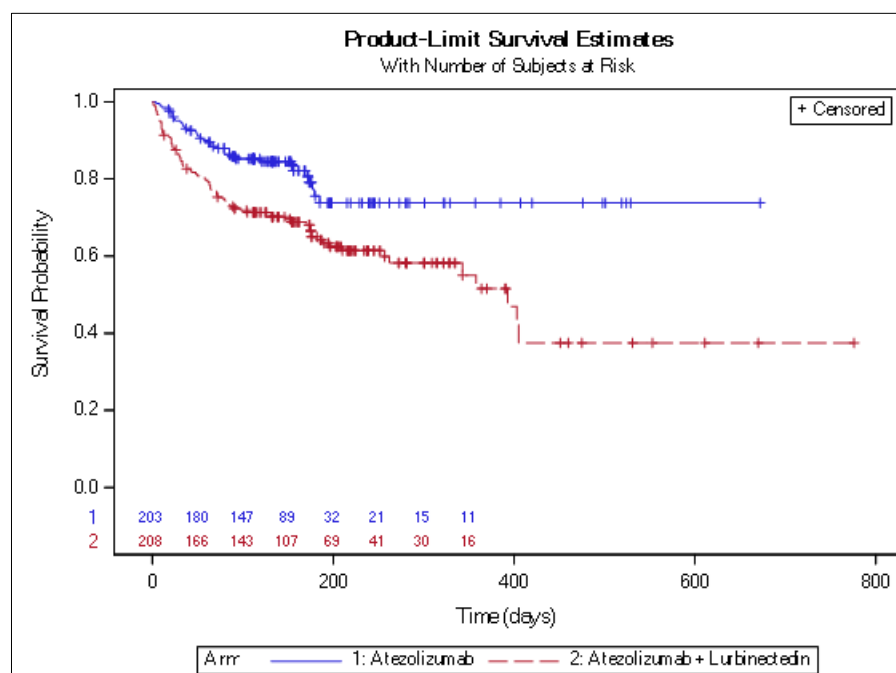


Abbildung 73: Kaplan-Meier plot for AE grade 3, patients not receiving PCI prior to randomization, IMforte trial, Safety Analysis Set, CCOD 29 July 2024

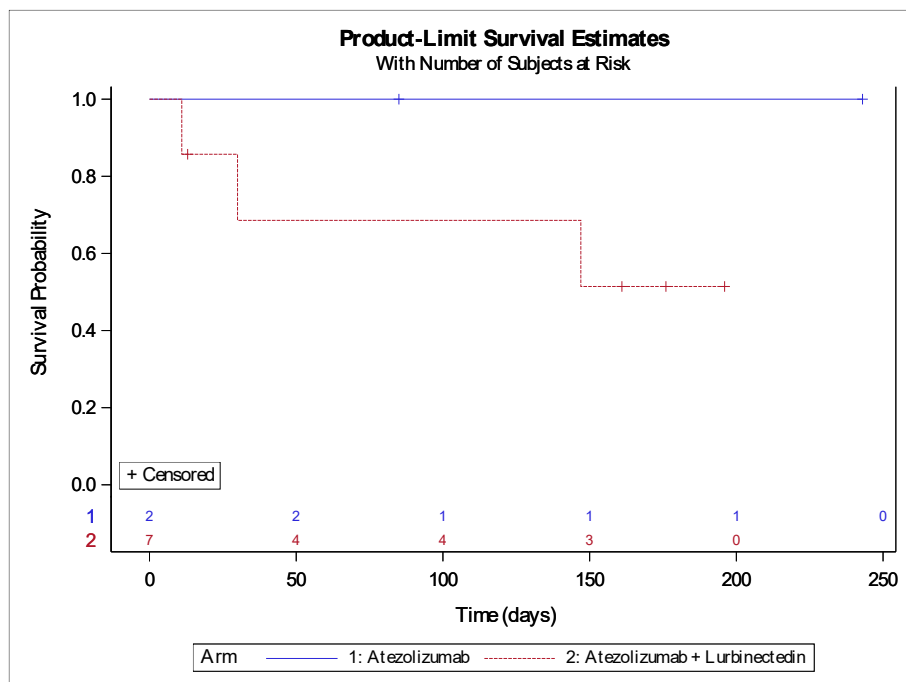


Abbildung 74: Kaplan-Meier plot for AE grade 3, patients with CR to induction treatment, IMforte trial, Safety Analysis Set, CCOD 29 July 2024

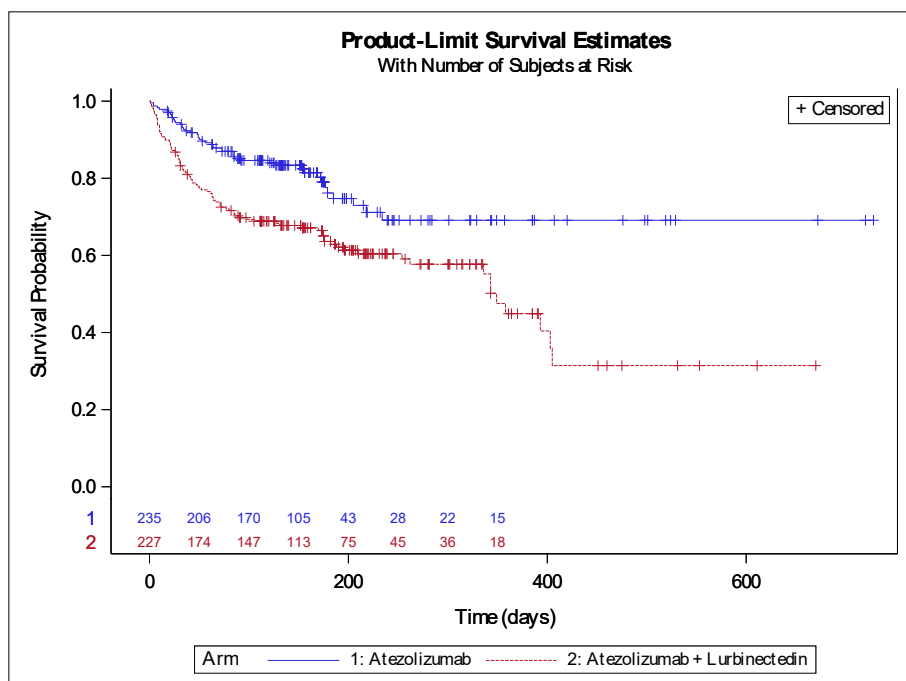


Abbildung 75: Kaplan-Meier plot for AE grade 3, patients with PR/SD to induction treatment, IMforte trial, Safety Analysis Set, CCOD 29 July 2024

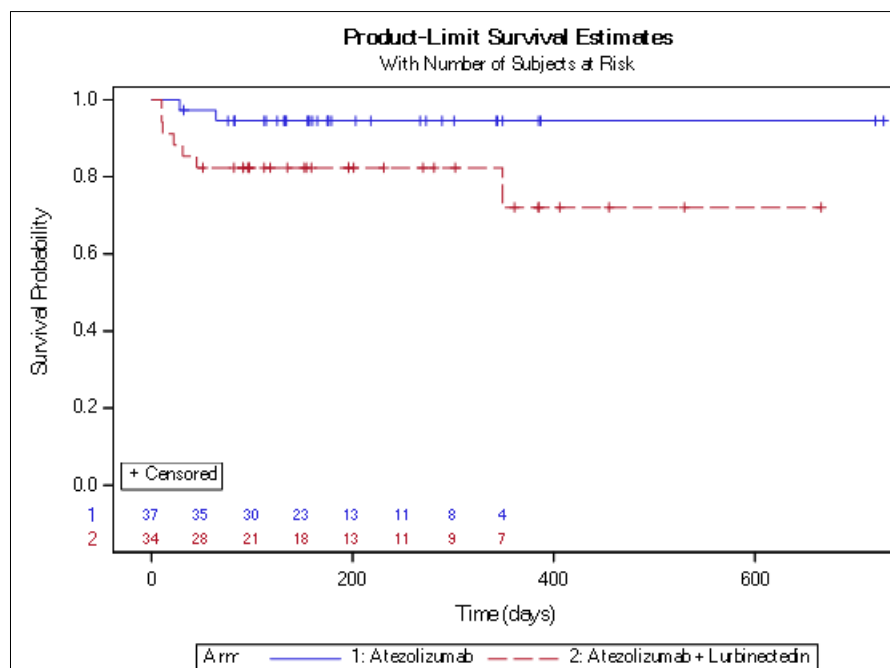


Abbildung 76: Kaplan-Meier plot for AE grade 4, patients receiving PCI prior to randomization, IMforte trial, Safety Analysis Set, CCOD 29 July 2024

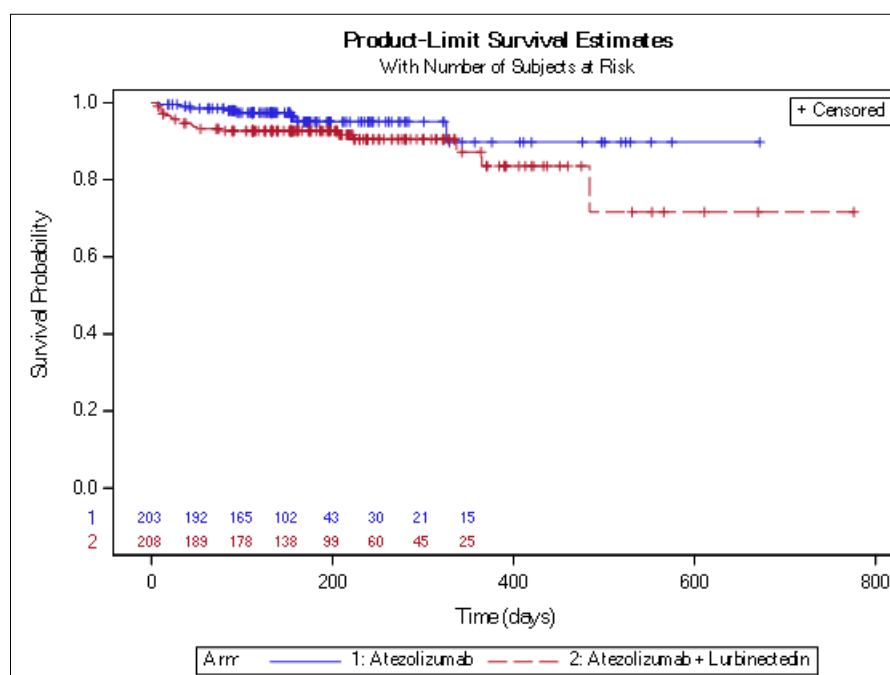


Abbildung 77: Kaplan-Meier plot for AE grade 4, patients not receiving PCI prior to randomization, IMforte trial, Safety Analysis Set, CCOD 29 July 2024

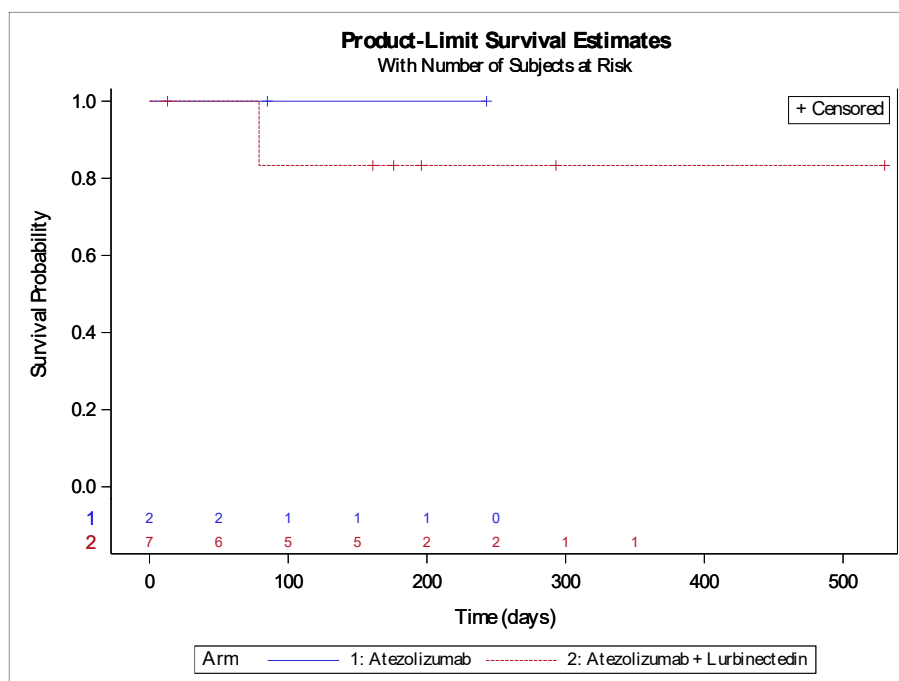


Abbildung 78: Kaplan-Meier plot for AE grade 4, patients with CR to induction treatment, IMforte trial, Safety Analysis Set, CCOD 29 July 2024

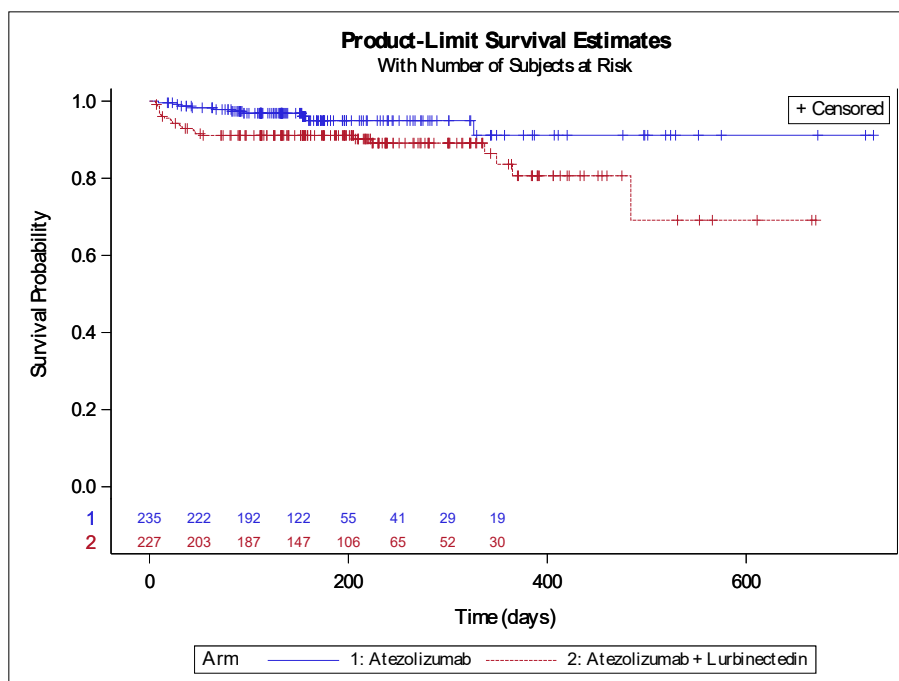


Abbildung 79: Kaplan-Meier plot for AE grade 4, patients with PR/SD to induction treatment, IMforte trial, Safety Analysis Set, CCOD 29 July 2024

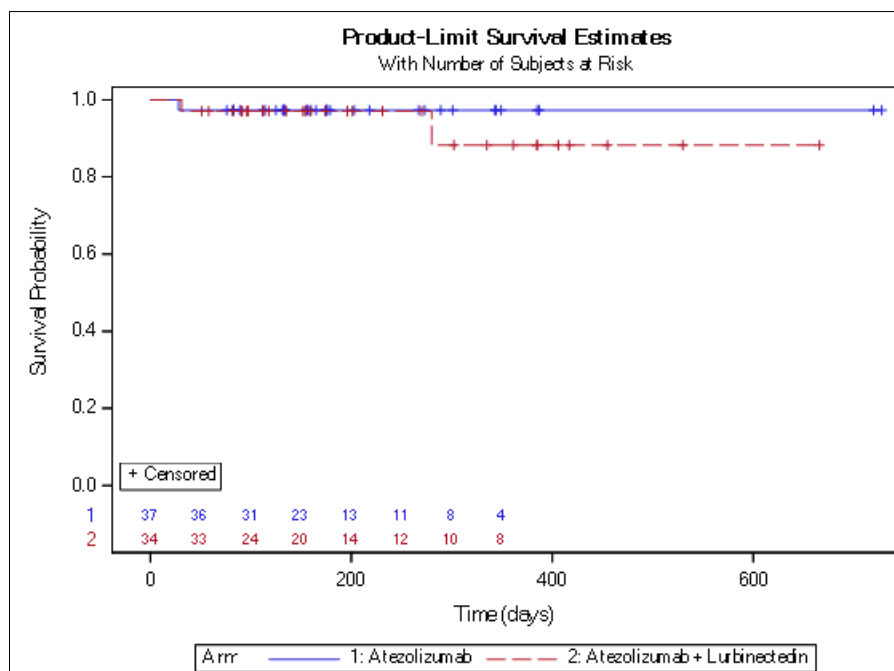


Abbildung 80: Kaplan-Meier plot for AE grade 5, patients receiving PCI prior to randomization, IMforte trial, Safety Analysis Set, CCOD 29 July 2024

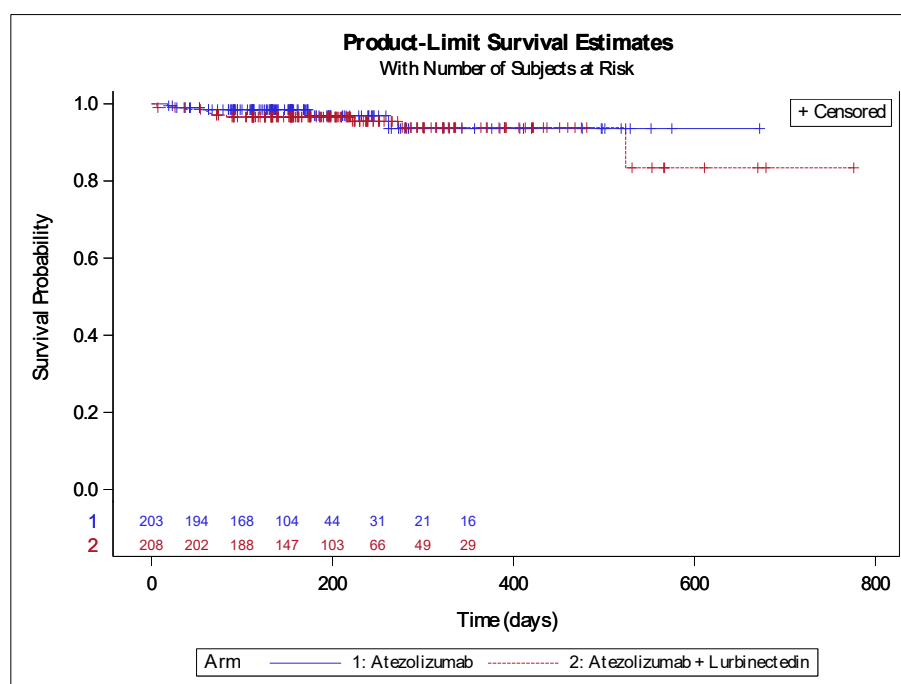


Abbildung 81: Kaplan-Meier plot for AE grade 5, patients not receiving PCI prior to randomization, IMforte trial, Safety Analysis Set, CCOD 29 July 2024

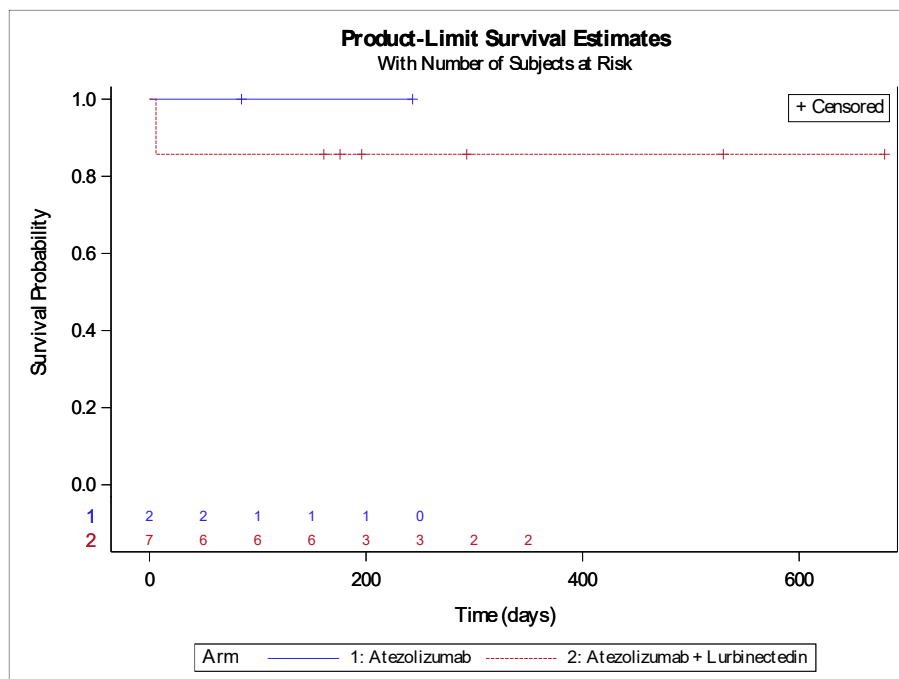


Abbildung 82: Kaplan-Meier plot for AE grade 5, patients with CR to induction treatment, IMforte trial, Safety Analysis Set, CCOD 29 July 2024

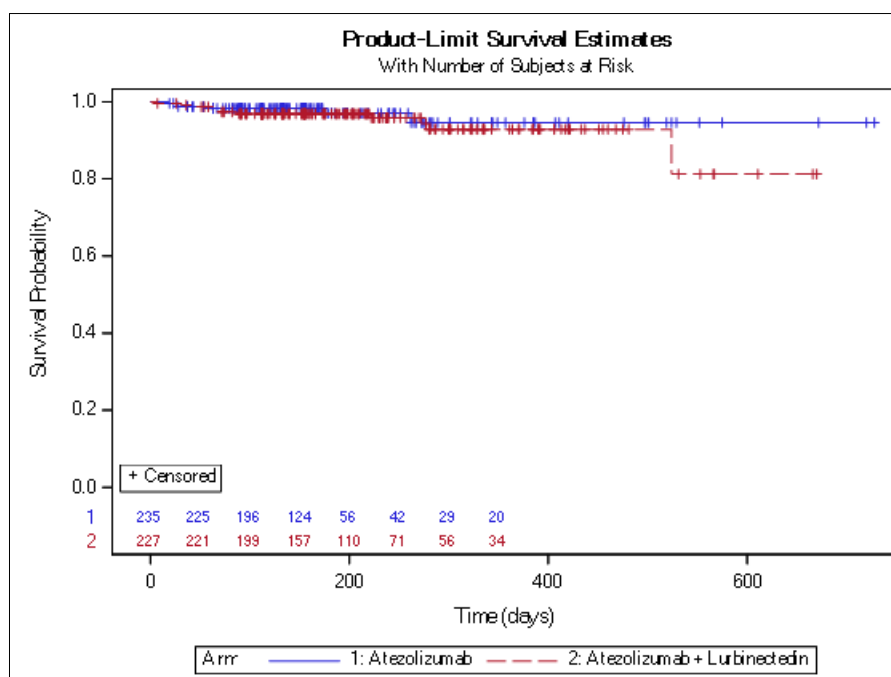


Abbildung 83: Kaplan-Meier plot for AE grade 5, patients with SD/PR to induction treatment, IMforte trial, Safety Analysis Set, CCOD 29 July 2024

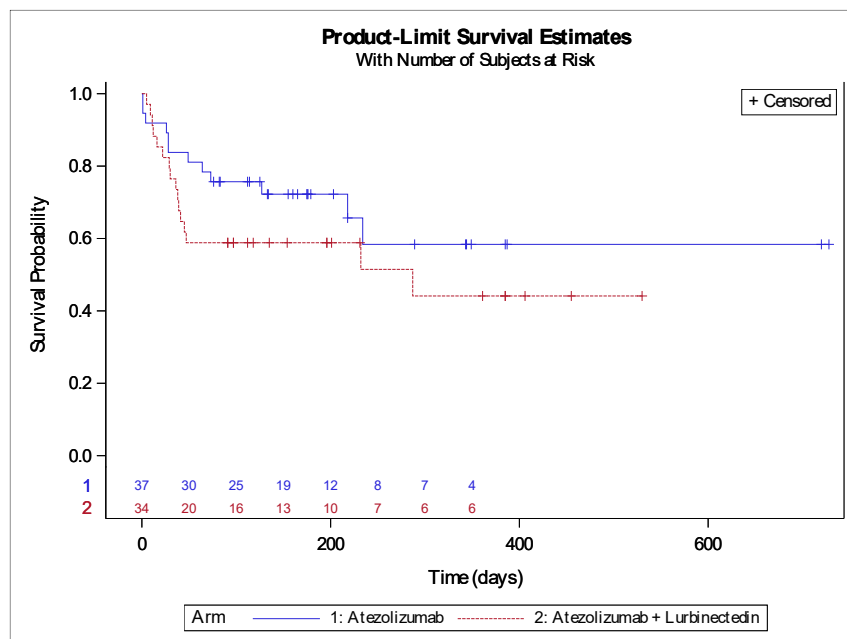


Abbildung 84: Kaplan-Meier plot for serious AE, patients receiving PCI prior to randomization, IMforte trial, Safety Analysis Set, CCOD 29 July 2024

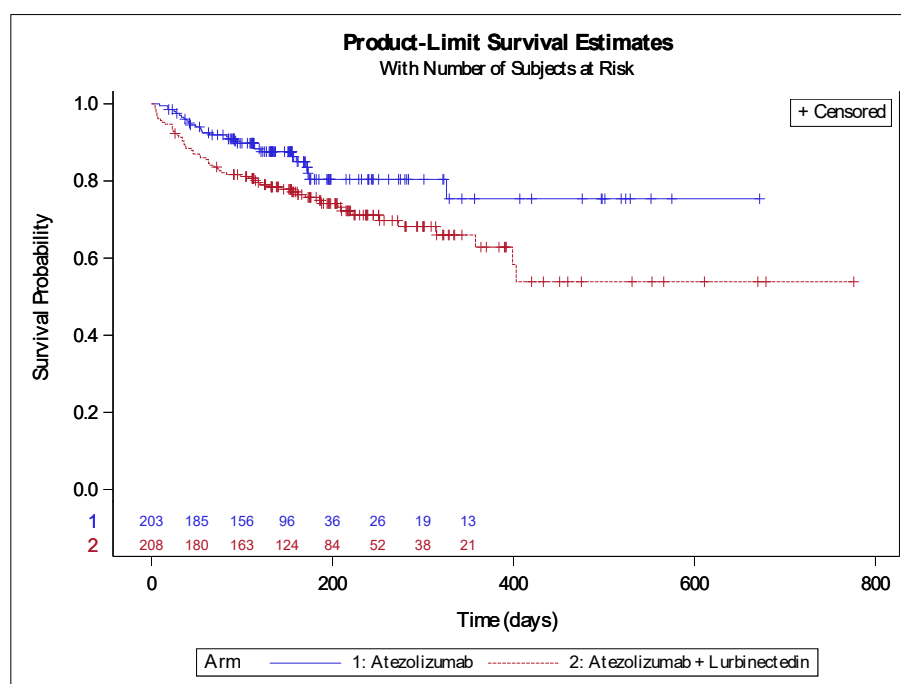


Abbildung 85: Kaplan-Meier plot for serious AE, patients not receiving PCI prior to randomization, IMforte trial, Safety Analysis Set, CCOD 29 July 2024

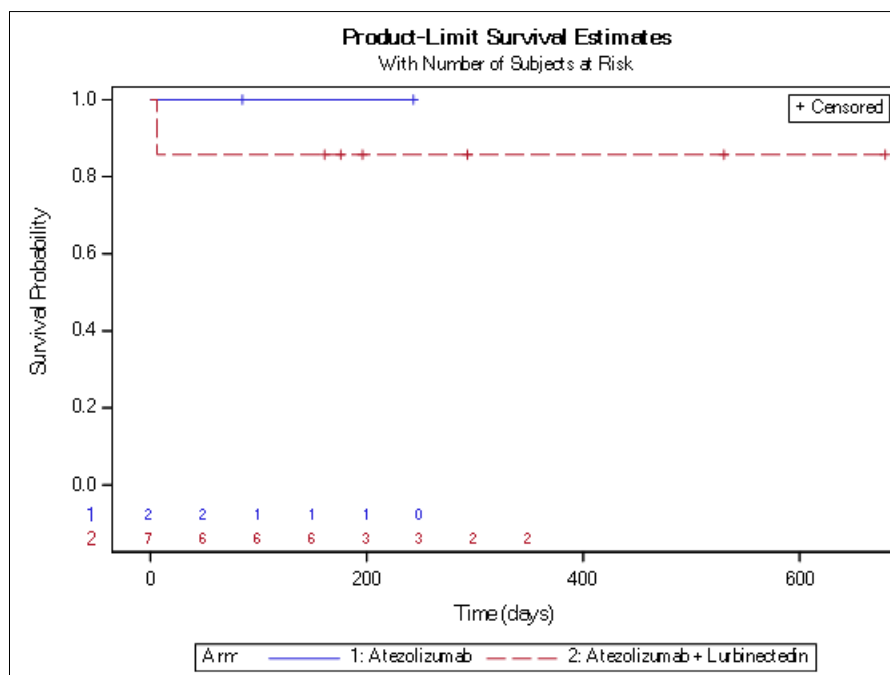


Abbildung 86: Kaplan-Meier plot for serious AE, patients with CR to induction treatment, IMforte trial, Safety Analysis Set, CCOD 29 July 2024

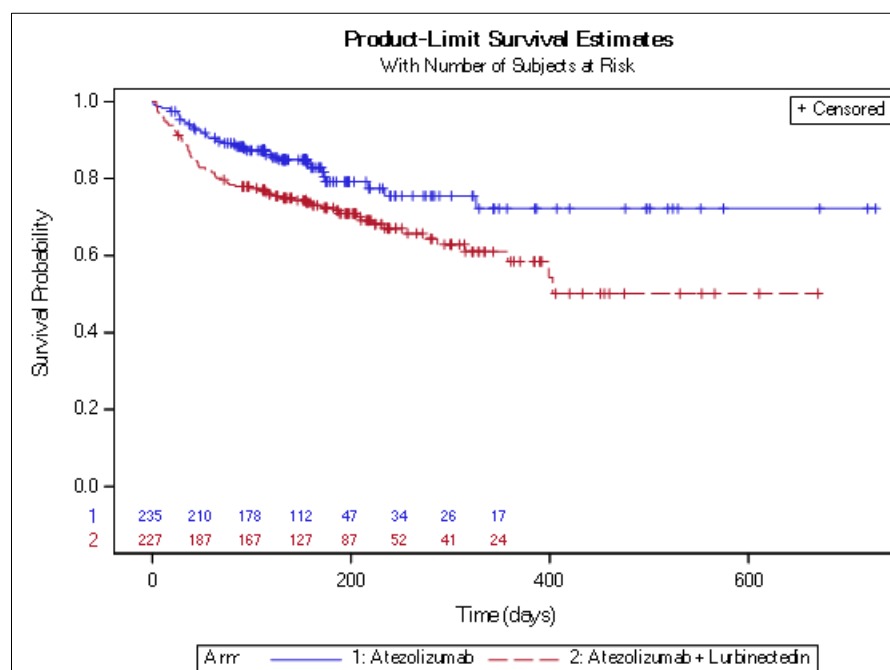


Abbildung 87: Kaplan-Meier plot for serious AE, patients with PR/SD to induction treatment, IMforte trial, Safety Analysis Set, CCOD 29 July 2024

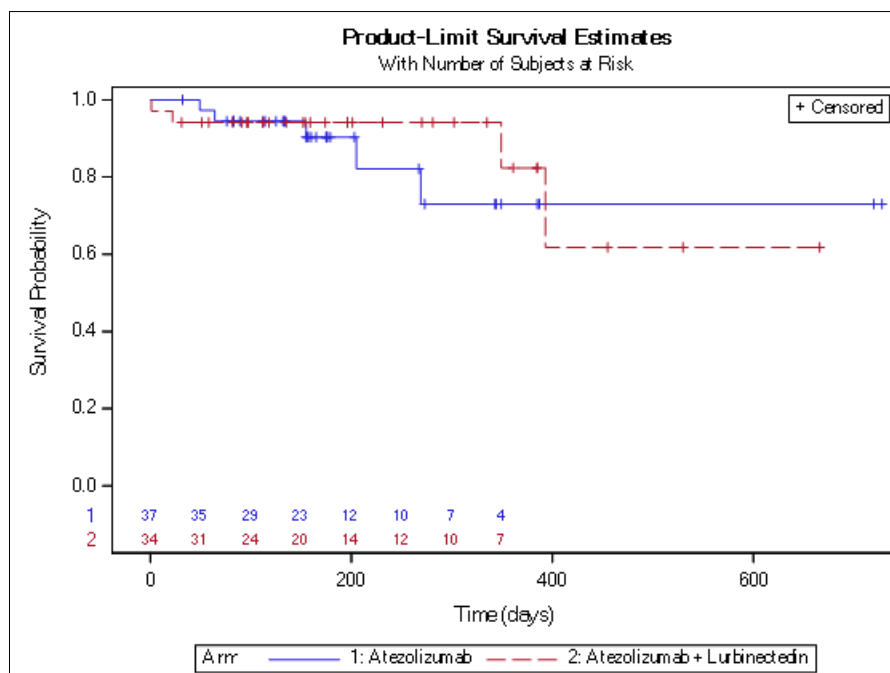


Abbildung 88: Kaplan-Meier plot for treatment discontinuation due to AE, patients receiving PCI prior to randomization, IMforte trial, Safety Analysis Set, CCOD 29 July 2024

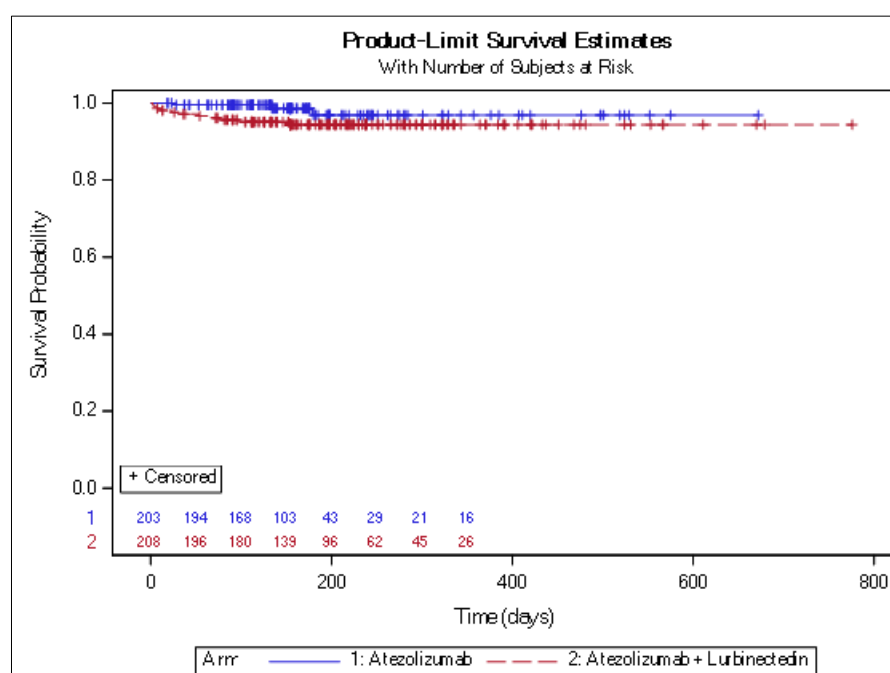


Abbildung 89: Kaplan-Meier plot for treatment discontinuation due to AE, patients not receiving PCI prior to randomization, IMforte trial, Safety Full Analysis Set, CCOD 29 July 2024

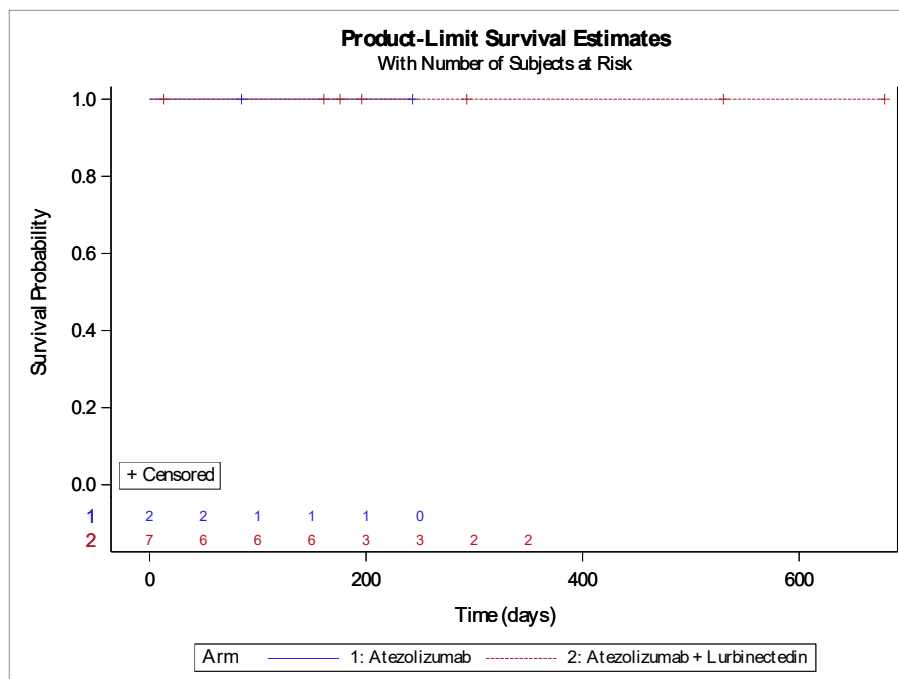


Abbildung 90: Kaplan-Meier plot for treatment discontinuation due to AE, patients with CR to induction treatment, IMforte trial, Safety Analysis Set, CCOD 29 July 2024

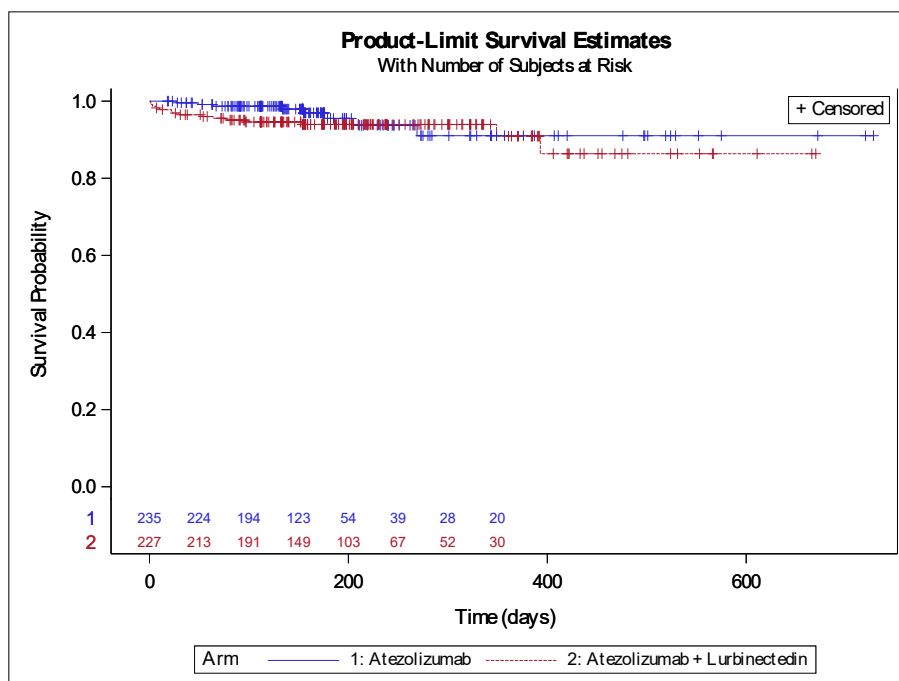


Abbildung 91: Kaplan-Meier plot for treatment discontinuation due to AE, patients with PR/SD to induction treatment, IMforte trial, Safety Analysis Set, CCOD 29 July 2024

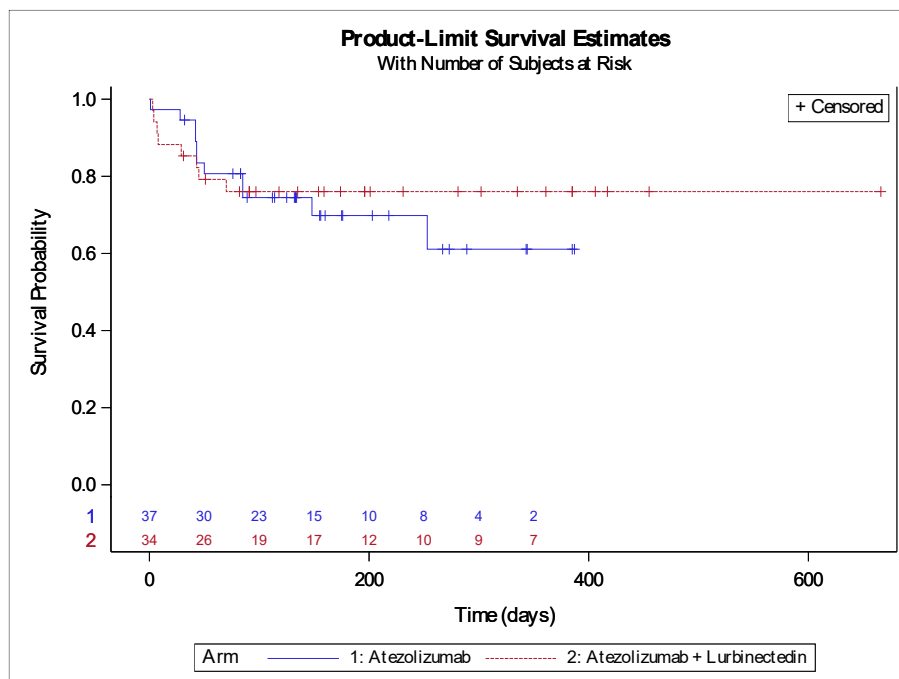


Abbildung 92: Kaplan-Meier plot for immune-related AE, patients receiving PCI prior to randomization, IMforte trial, Safety Analysis Set, CCOD 29 July 2024

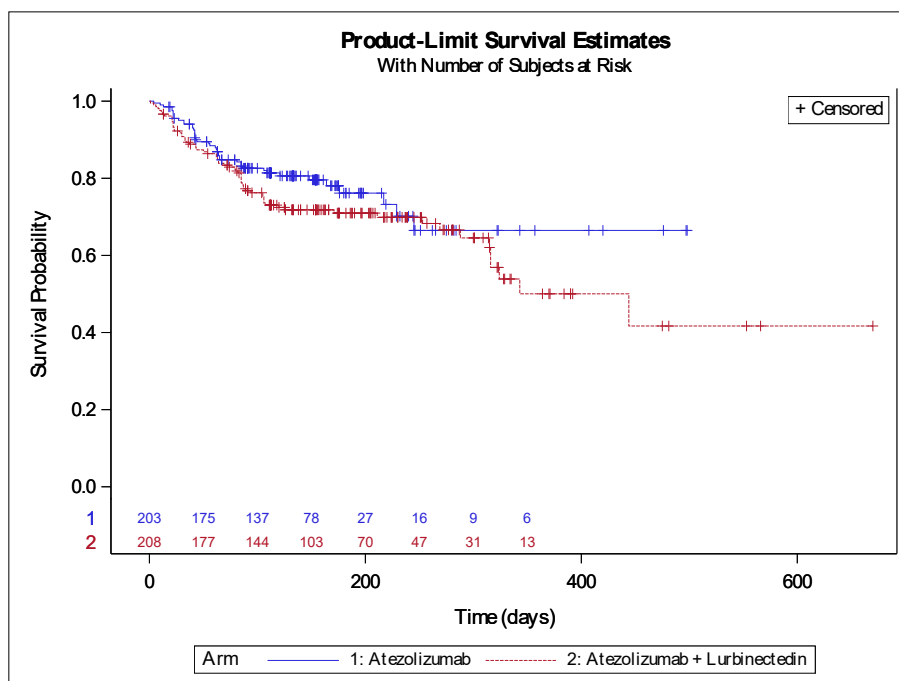


Abbildung 93: Kaplan-Meier plot for immune-related AE, patients not receiving PCI prior to randomization, IMforte trial, Safety Analysis Set, CCOD 29 July 2024

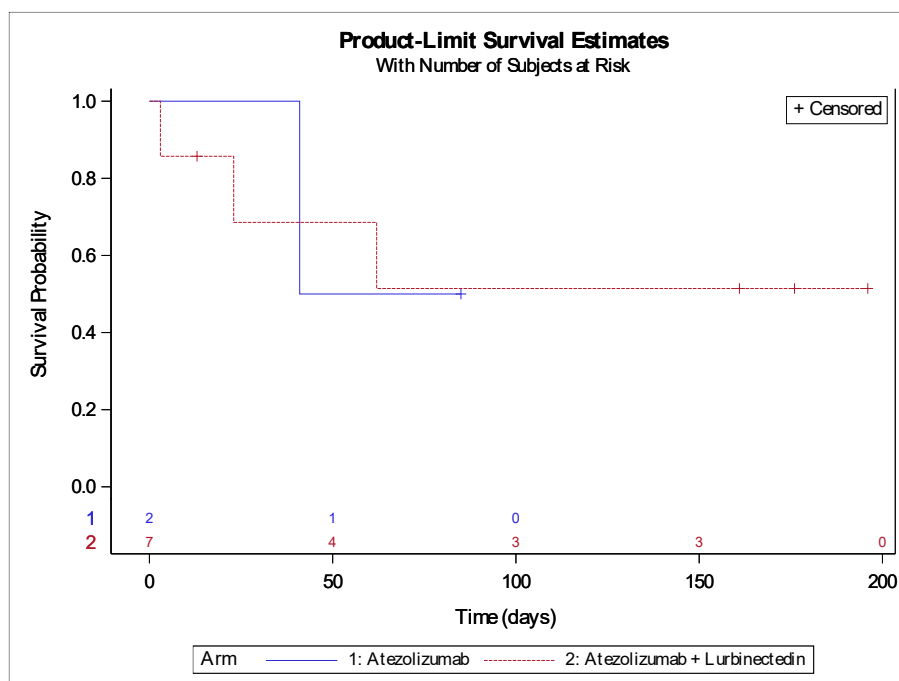


Abbildung 94: Kaplan-Meier plot for immune-related AE, patients with CR to induction treatment, IMforte trial, Safety Analysis Set, CCOD 29 July 2024

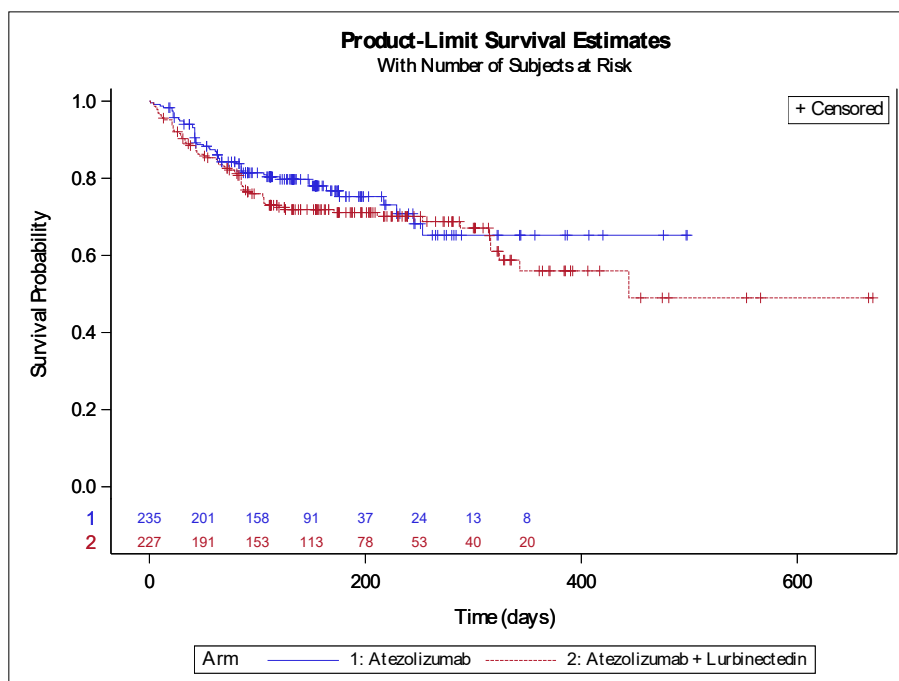


Abbildung 95: Kaplan-Meier plot for immune-related AE, patients with PR/SD to induction treatment, IMforte trial, Safety Analysis Set, CCOD 29 July 2024

**2 Unerwünschte Ereignisse (Explorativer Datenschnitt 12 Februar 2025)**

Tabelle 9: Safety outcomes (time-to-event): lurbinectedin + atezolizumab vs. atezolizumab (IMforte)

| Time point<br>Outcome<br>Analysis          | Lurbinectedin + atezolizumab |                                                                                                       | Atezolizumab       |                                                                                                       | Lurbinectedin + atezolizumab vs.<br>atezolizumab |
|--------------------------------------------|------------------------------|-------------------------------------------------------------------------------------------------------|--------------------|-------------------------------------------------------------------------------------------------------|--------------------------------------------------|
|                                            | N/N <sup>Cen</sup>           | Median time to event in<br>days <sup>a</sup><br>[95% CI] <sup>b</sup><br>patients with event<br>n (%) | N/N <sup>Cen</sup> | Median time to event in<br>days <sup>a</sup><br>[95% CI] <sup>b</sup><br>patients with event<br>n (%) | HR [95% CI] <sup>c</sup><br>p-value <sup>d</sup> |
| Total AE                                   | 242/7                        | 10 [9; 11]<br>235 (97.1)                                                                              | 240/44             | 35 [24; 43]<br>196 (81.7)                                                                             | 2.15 [1.76; 2.62]<br><.0001                      |
| Severe AE<br>[CTCAE]                       |                              |                                                                                                       |                    |                                                                                                       |                                                  |
| Grade ≥3                                   | 242/130                      | 336 [254; 403]<br>112 (46.3)                                                                          | 240/175            | NE [326; NE]<br>65 (27.1)                                                                             | 1.69 [1.24; 2.30]<br>0.0007                      |
| Grade 5<br>(death)                         | 242/230                      | NE [NE; NE]<br>12 (5.0)                                                                               | 240/234            | NE [NE; NE]<br>6 (2.5)                                                                                | 1.67 [0.62; 4.49]<br>0.3019                      |
| Serious AE                                 | 242/159                      | 512 [378; NE]<br>83 (34.3)                                                                            | 240/197            | NE [NE; NE]<br>43 (17.9)                                                                              | 1.77 [1.22; 2.56]<br>0.0023                      |
| Treatment<br>discontinuation<br>due to AE  | 242/225                      | NE [NE; NE]<br>17 (7.0)                                                                               | 240/230            | NE [NE; NE]<br>10 (4.2)                                                                               | 1.43 [0.65; 3.14]<br>0.3703                      |
| Immune-related<br>AE <sup>e</sup>          | 242/157                      | 444 [324; NE]<br>85 (35.1)                                                                            | 240/182            | NE [400; NE]<br>58 (24.2)                                                                             | 1.27 [0.91; 1.79]<br>0.1591                      |
| CCOD: 12 February 2025; NE: not estimable. |                              |                                                                                                       |                    |                                                                                                       |                                                  |

| Time point<br>Outcome<br>Analysis                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          | Lurbinectedin + atezolizumab |                                                                                                       | Atezolizumab       |                                                                                                       | Lurbinectedin + atezolizumab vs.<br>atezolizumab |
|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------|-------------------------------------------------------------------------------------------------------|--------------------|-------------------------------------------------------------------------------------------------------|--------------------------------------------------|
|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            | N/N <sup>Cen</sup>           | Median time to event in<br>days <sup>a</sup><br>[95% CI] <sup>b</sup><br>patients with event<br>n (%) | N/N <sup>Cen</sup> | Median time to event in<br>days <sup>a</sup><br>[95% CI] <sup>b</sup><br>patients with event<br>n (%) | HR [95% CI] <sup>c</sup><br>p-value <sup>d</sup> |
| <p>a: summaries of duration (median) are Kaplan-Meier estimates.</p> <p>b: 95% CIs for the median were computed using the method of Brookmeyer and Crowley.</p> <p>c: hazard ratios were estimated using a stratified Cox proportional hazard model. The stratification factors are ECOG PS at randomization (0 vs. 1), LDH at randomization (<math>\leq</math>ULN vs <math>&gt;</math>ULN) via local laboratory test, presence of liver metastases at enrollment (yes vs. no), and prior receipt of PCI (yes vs. no).</p> <p>d: p-value based on the log rank test.</p> <p>e: specific AE, as requested by the assessment scope. Immune-related AE were calculated as a combined endpoint comprising the following immune-mediated AE: adrenal insufficiency, colitis, diabetes mellitus, encephalitis, Guillain-Barre syndrome, hepatitis (diagnosis and lab abnormalities), hepatitis (diagnosis), hepatitis (lab abnormalities), hyperthyroidism, hypothyroidism, meningoencephalitis, myositis, myositis (myositis + rhabdomyolysis) nephritis, ocular inflammatory toxicity, pancreatitis, pericardial disorders, pneumonitis, rhabdomyolysis, rash, severe cutaneous reactions, and vasculitis.</p> |                              |                                                                                                       |                    |                                                                                                       |                                                  |

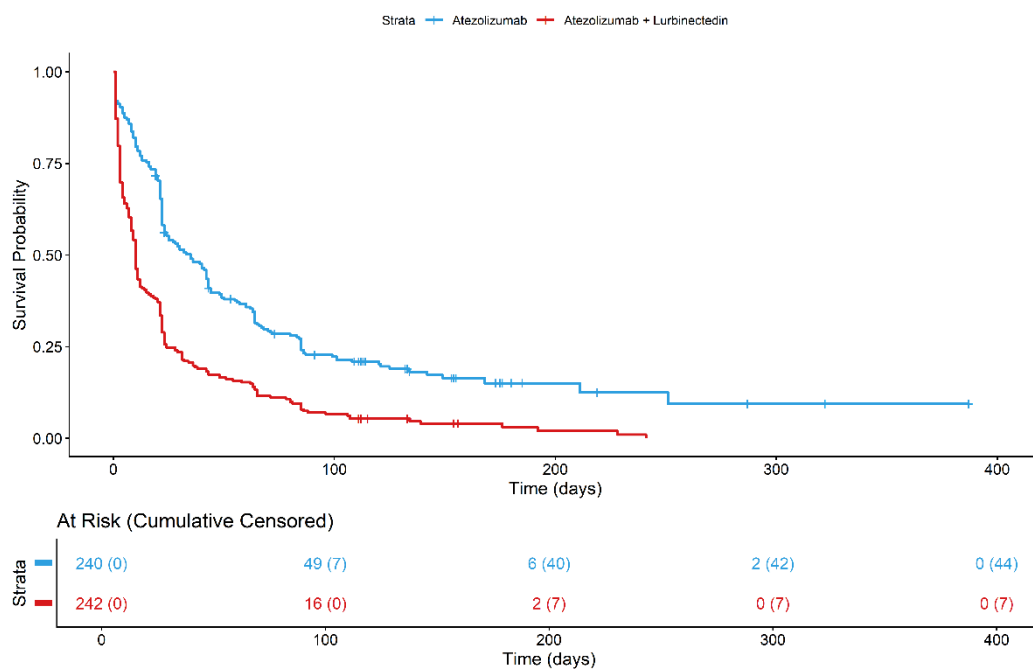


Abbildung 96: Kaplan-Meier plot for total AE, IMforte trial, Safety Analysis Set, CCOD 12 February 2025

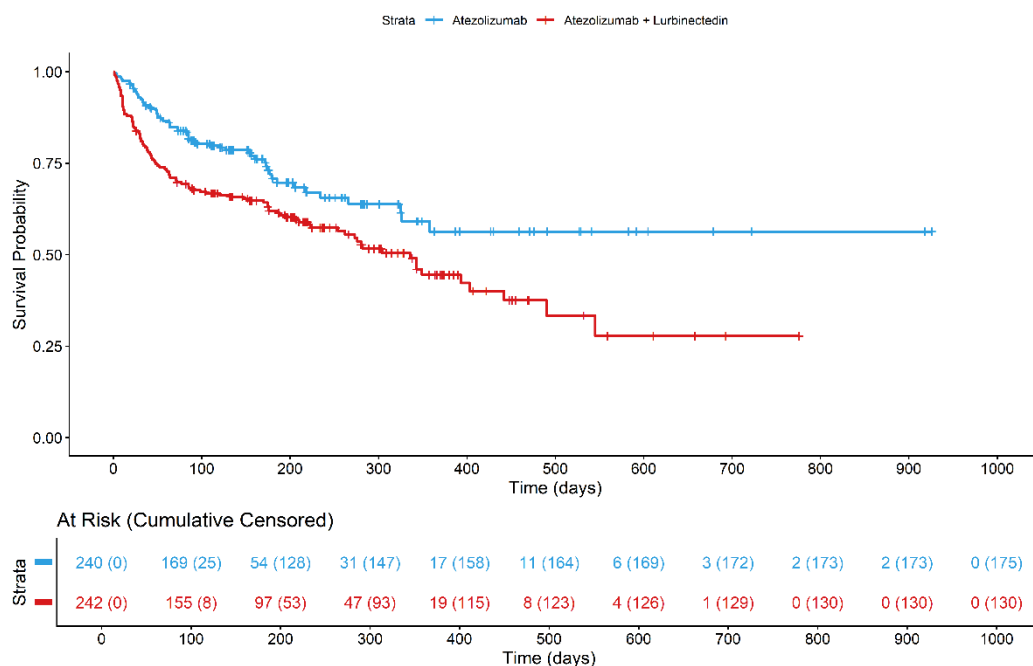


Abbildung 97: Kaplan-Meier plot for severe AE, IMforte trial, Safety Analysis Set, CCOD 12 February 2025

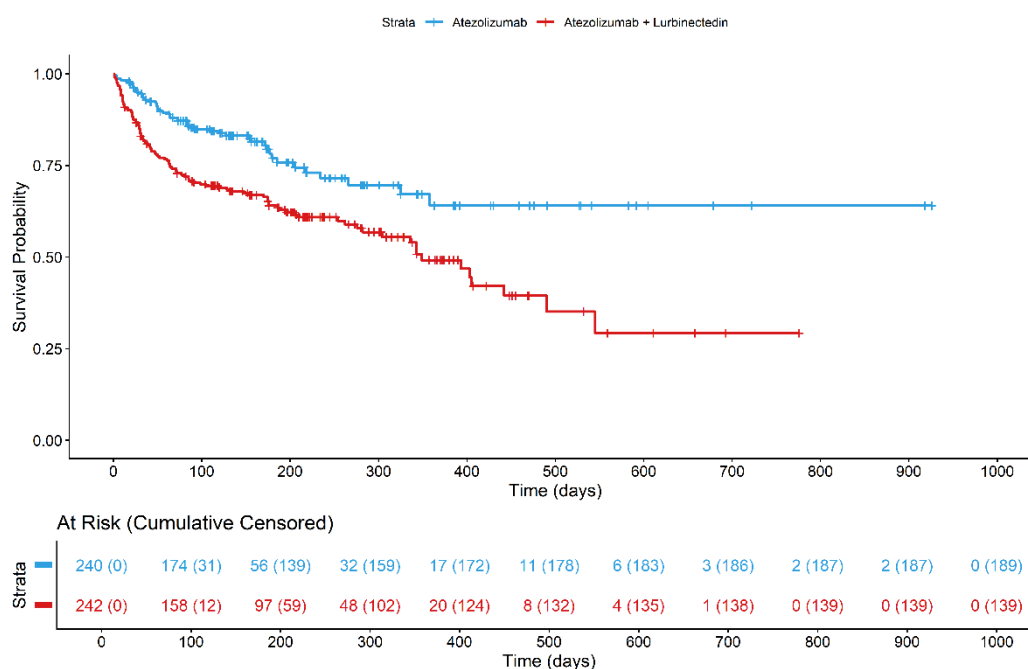


Abbildung 98: Kaplan-Meier plot for grade 3 AE, IMforte trial, Safety Analysis Set, CCOD 12 February 2025

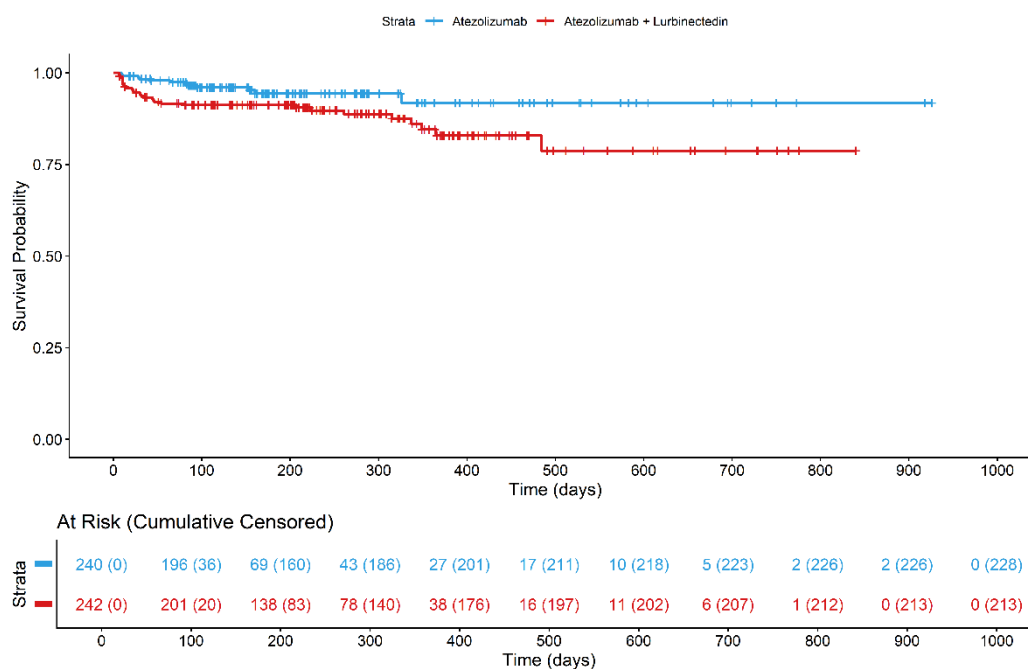


Abbildung 99: Kaplan-Meier plot for grade 4 AE, IMforte trial, Safety Analysis Set, CCOD 12 February 2025

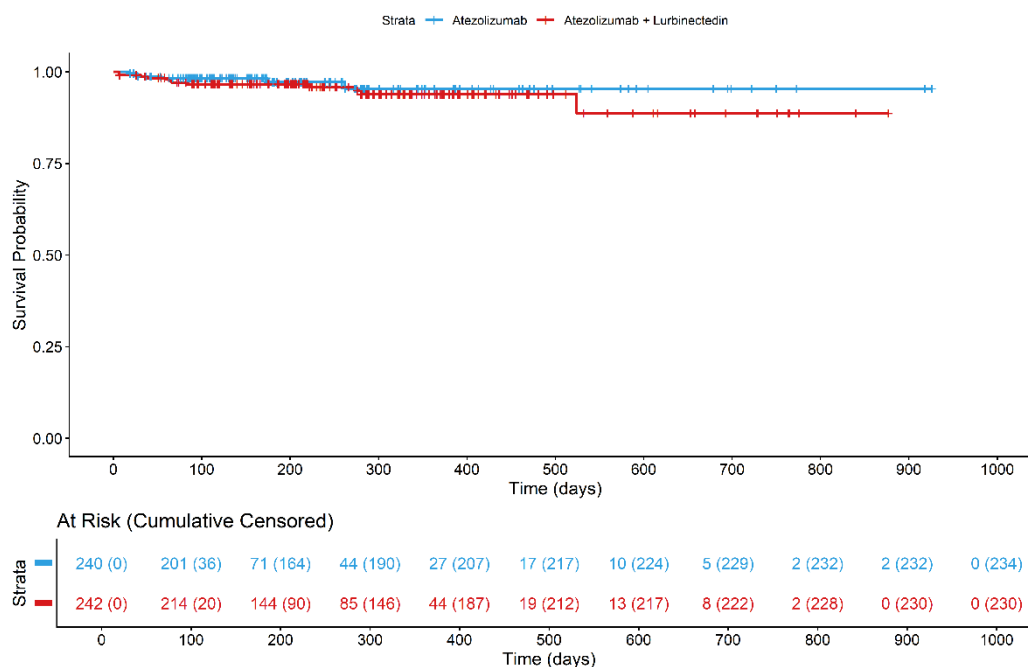


Abbildung 100: Kaplan-Meier plot for grade 5 AE, IMforte trial, Safety Analysis Set, CCOD 12 February 2025

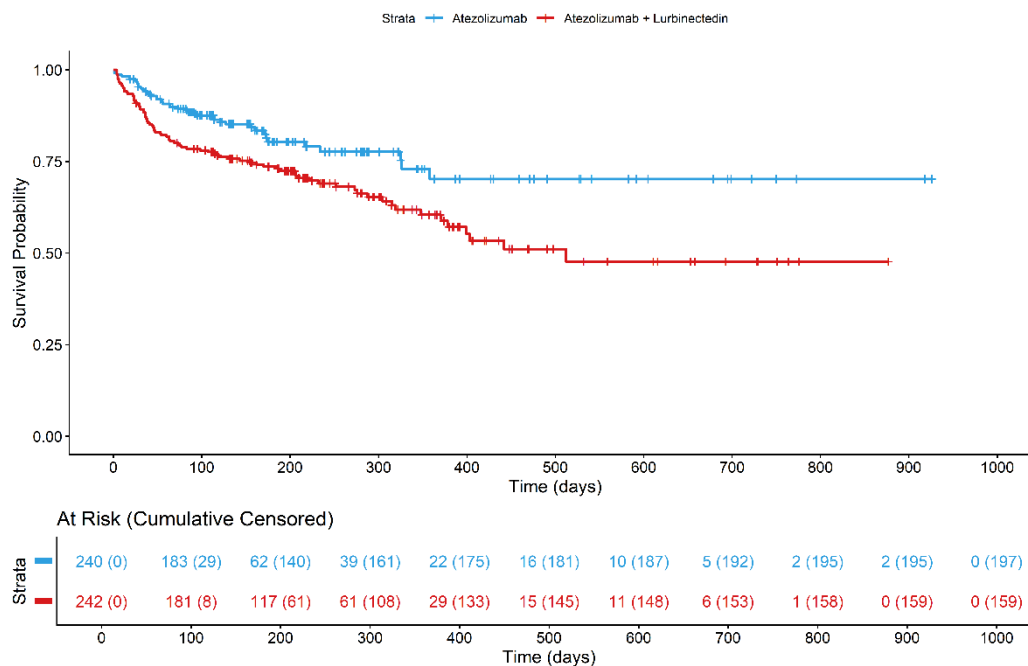


Abbildung 101: Kaplan-Meier plot for serious AE, IMforte trial, Safety Analysis Set, CCOD 12 February 2025

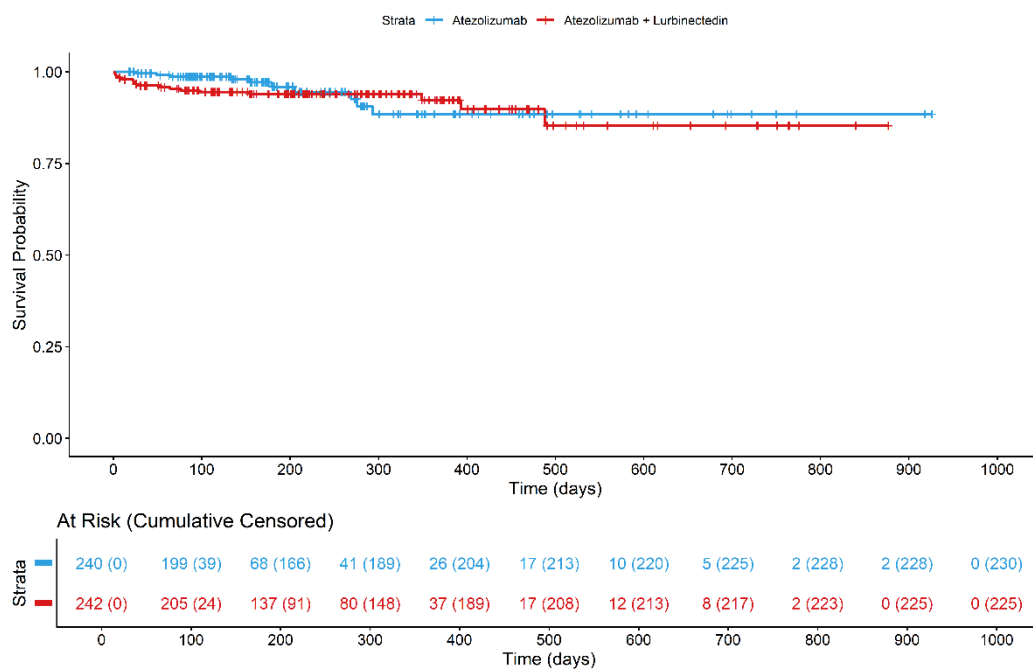


Abbildung 102: Kaplan-Meier plot for treatment discontinuation due to AE, IMforte trial, Safety Analysis Set, CCOD 12 February 2025

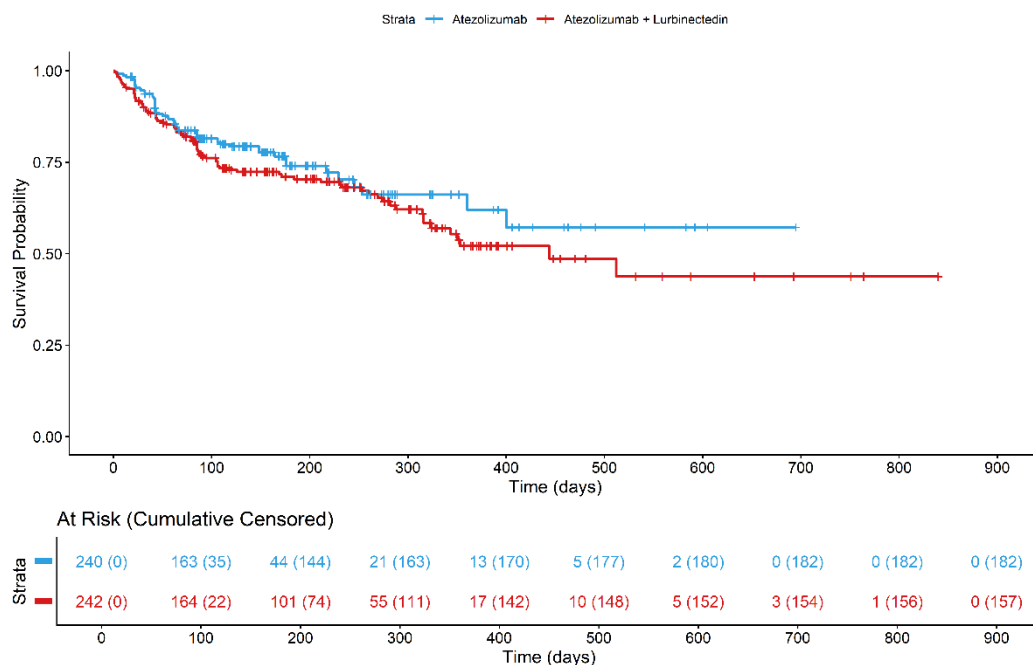


Abbildung 103: Kaplan-Meier plot for immune-related AE, IMforte trial, Safety Analysis Set, CCOD 12 February 2025

Tabelle 10: AE of any severity by SOC and PT including effect estimates

| Endpoint<br>SOC<br>PT                | Lurbinectedin + atezolizumab |                                                                                                    | Atezolizumab       |                                                                                                    | Lurbinectedin + atezolizumab vs. atezolizumab    |
|--------------------------------------|------------------------------|----------------------------------------------------------------------------------------------------|--------------------|----------------------------------------------------------------------------------------------------|--------------------------------------------------|
|                                      | N/N <sup>Cen</sup>           | Median time to event in days <sup>a</sup><br>[95% CI] <sup>b</sup><br>patients with event<br>n (%) | N/N <sup>Cen</sup> | Median time to event in days <sup>a</sup><br>[95% CI] <sup>b</sup><br>patients with event<br>n (%) | HR [95% CI] <sup>c</sup><br>p-value <sup>d</sup> |
| Blood and lymphatic system disorders | 242/135                      | 349 [241; 512]<br>107 (44.2)                                                                       | 240/217            | NE [NE; NE]<br>23 (9.6)                                                                            | 5.249 [3.338; 8.254]<br><.0001                   |
| Anemia                               | 242/160                      | 512 [400; NE]<br>82 (33.9)                                                                         | 240/223            | NE [NE; NE]<br>17 (7.1)                                                                            | 4.910 [2.908; 8.290]<br><.0001                   |
| Neutropenia                          | 242/212                      | NE [NE; NE]<br>30 (12.4)                                                                           | 240/236            | NE [NE; NE]<br>4 (1.7)                                                                             | 6.934 [2.438; 19.718]<br><.0001                  |
| Thrombocytopenia                     | 242/211                      | NE [NE; NE]<br>31 (12.8)                                                                           | 240/236            | NE [NE; NE]<br>4 (1.7)                                                                             | 7.642 [2.693; 21.689]<br><.0001                  |
| Cardiac disorders                    | 242/228                      | NE [NE; NE]<br>14 (5.8)                                                                            | 240/236            | NE [NE; NE]<br>4 (1.7)                                                                             | 3.125 [1.024; 9.532]<br>0.0349                   |
| Endocrine disorders                  | 242/215                      | NE [NE; NE]<br>27 (11.2)                                                                           | 240/216            | NE [NE; NE]<br>24 (10.0)                                                                           | 0.992 [0.570; 1.726]<br>0.9759                   |
| Hypothyroidism                       | 242/223                      | NE [NE; NE]<br>19 (7.9)                                                                            | 240/223            | NE [NE; NE]<br>17 (7.1)                                                                            | 0.954 [0.493; 1.846]<br>0.8888                   |
| Gastrointestinal disorders           | 242/98                       | 84 [44; 157]<br>144 (59.5)                                                                         | 240/176            | NE [420.000; NE]<br>64 (26.7)                                                                      | 2.947 [2.191; 3.964]<br><.0001                   |
| Abdominal pain                       | 242/230                      | NE [NE; NE]<br>12 (5.0)                                                                            | 240/236            | NE [NE; NE]<br>4 (1.7)                                                                             | 2.702 [0.868; 8.412]<br>0.0741                   |

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

| Endpoint<br>SOC<br>PT                                | Lurbinectedin + atezolizumab |                                                                                                    | Atezolizumab       |                                                                                                    | Lurbinectedin + atezolizumab vs. atezolizumab    |
|------------------------------------------------------|------------------------------|----------------------------------------------------------------------------------------------------|--------------------|----------------------------------------------------------------------------------------------------|--------------------------------------------------|
|                                                      | N/N <sup>Cen</sup>           | Median time to event in days <sup>a</sup><br>[95% CI] <sup>b</sup><br>patients with event<br>n (%) | N/N <sup>Cen</sup> | Median time to event in days <sup>a</sup><br>[95% CI] <sup>b</sup><br>patients with event<br>n (%) | HR [95% CI] <sup>c</sup><br>p-value <sup>d</sup> |
| Constipation                                         | 242/211                      | NE [NE; NE]<br>31 (12.8)                                                                           | 240/225            | NE [NE; NE]<br>15 (6.3)                                                                            | 1.880 [1.012; 3.493]<br>0.0422                   |
| Diarrhea                                             | 242/204                      | NE [NE; NE]<br>38 (15.7)                                                                           | 240/220            | NE [NE; NE]<br>20 (8.3)                                                                            | 1.736 [1.007; 2.992]<br>0.0443                   |
| Nausea                                               | 242/151                      | NE [NE; NE]<br>91 (37.6)                                                                           | 240/229            | NE [NE; NE]<br>11 (4.6)                                                                            | 9.680<br>[5.171; 18.121]<br><.0001               |
| Vomiting                                             | 242/206                      | NE [775; NE]<br>36 (14.9)                                                                          | 240/234            | NE [NE; NE]<br>6 (2.5)                                                                             | 5.886<br>[2.476; 13.989]<br><.0001               |
| General disorders and administration site conditions | 242/126                      | 233 [170; 434]<br>116 (47.9)                                                                       | 240/173            | 610.000 [399.000; NE]<br>67 (27.9)                                                                 | 1.896<br>[1.401; 2.565]<br><.0001                |
| Asthenia                                             | 242/208                      | NE [772; NE]<br>34 (14.0)                                                                          | 240/224            | NE [NE; NE]<br>16 (6.7)                                                                            | 1.888<br>[1.038; 3.432]<br>0.0342                |
| Chest pain                                           | 242/234                      | NE [NE; NE]<br>8 (3.3)                                                                             | 240/228            | NE [NE; NE]<br>12 (5.0)                                                                            | 0.572<br>[0.233; 1.407]<br>0.2183                |

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

| Endpoint<br>SOC<br>PT             | Lurbinectedin + atezolizumab |                                                                                                    | Atezolizumab       |                                                                                                    | Lurbinectedin + atezolizumab vs. atezolizumab    |
|-----------------------------------|------------------------------|----------------------------------------------------------------------------------------------------|--------------------|----------------------------------------------------------------------------------------------------|--------------------------------------------------|
|                                   | N/N <sup>Cen</sup>           | Median time to event in days <sup>a</sup><br>[95% CI] <sup>b</sup><br>patients with event<br>n (%) | N/N <sup>Cen</sup> | Median time to event in days <sup>a</sup><br>[95% CI] <sup>b</sup><br>patients with event<br>n (%) | HR [95% CI] <sup>c</sup><br>p-value <sup>d</sup> |
| Fatigue                           | 242/191                      | NE [NE; NE]<br>51 (21.1)                                                                           | 240/220            | NE [NE; NE]<br>20 (8.3)                                                                            | 2.541<br>[1.513; 4.266]<br>0.0003                |
| Oedema peripheral                 | 242/229                      | NE [NE; NE]<br>13 (5.4)                                                                            | 240/236            | NE [NE; NE]<br>4 (1.7)                                                                             | 2.754 [0.893; 8.496]<br>0.0663                   |
| Pyrexia                           | 242/229                      | NE [NE; NE]<br>13 (5.4)                                                                            | 240/238            | NE [NE; NE]<br>2 (0.8)                                                                             | 5.859<br>[1.317; 26.073]<br>0.0086               |
| Infections and infestations       | 242/143                      | 350 [303; 412]<br>99 (40.9)                                                                        | 240/176            | 539.000 [328.000; NE]<br>64 (26.7)                                                                 | 1.410 [1.028; 1.934]<br>0.0325                   |
| COVID-19                          | 242/225                      | NE [NE; NE]<br>17 (7.0)                                                                            | 240/236            | NE [NE; NE]<br>4 (1.7)                                                                             | 3.696<br>[1.239; 11.028]<br>0.0121               |
| Pneumonia                         | 242/232                      | NE [NE; NE]<br>10 (4.1)                                                                            | 240/226            | NE [NE; NE]<br>14 (5.8)                                                                            | 0.589 [0.260; 1.337]<br>0.2009                   |
| Upper respiratory tract infection | 242/230                      | NE [NE; NE]<br>12 (5.0)                                                                            | 240/230            | 871.000 [871.000; NE]<br>10 (4.2)                                                                  | 1.050 [0.450; 2.451]<br>0.9101                   |
| Urinary tract infection           | 242/230                      | NE [NE; NE]<br>12 (5.0)                                                                            | 240/235            | NE [NE; NE]<br>5 (2.1)                                                                             | 2.064 [0.723; 5.887]<br>0.1664                   |

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

| Endpoint<br>SOC<br>PT                          | Lurbinectedin + atezolizumab |                                                                                                    | Atezolizumab       |                                                                                                    | Lurbinectedin + atezolizumab vs. atezolizumab    |
|------------------------------------------------|------------------------------|----------------------------------------------------------------------------------------------------|--------------------|----------------------------------------------------------------------------------------------------|--------------------------------------------------|
|                                                | N/N <sup>Cen</sup>           | Median time to event in days <sup>a</sup><br>[95% CI] <sup>b</sup><br>patients with event<br>n (%) | N/N <sup>Cen</sup> | Median time to event in days <sup>a</sup><br>[95% CI] <sup>b</sup><br>patients with event<br>n (%) | HR [95% CI] <sup>c</sup><br>p-value <sup>d</sup> |
| Injury, poisoning and procedural complications | 242/227                      | 775 [775; NE]<br>15 (6.2)                                                                          | 240/231            | NE [NE; NE]<br>9 (3.8)                                                                             | 1.351 [0.587; 3.107]<br>0.4778                   |
| Investigations                                 | 242/152                      | NE [308; NE]<br>90 (37.2)                                                                          | 240/189            | NE [400.000; NE]<br>51 (21.3)                                                                      | 1.717 [1.213; 2.429]<br>0.0020                   |
| Alanine aminotransferase increased             | 242/226                      | NE [NE; NE]<br>16 (6.6)                                                                            | 240/227            | NE [NE; NE]<br>13 (5.4)                                                                            | 1.075 [0.514; 2.250]<br>0.8467                   |
| Aspartate aminotransferase increased           | 242/225                      | NE [NE; NE]<br>17 (7.0)                                                                            | 240/227            | NE [NE; NE]<br>13 (5.4)                                                                            | 1.089 [0.525; 2.260]<br>0.8174                   |
| Blood creatinine phosphokinase increased       | 242/237                      | NE [NE; NE]<br>5 (2.1)                                                                             | 240/227            | NE [NE; NE]<br>13 (5.4)                                                                            | 0.306 [0.108; 0.866]<br>0.0185                   |
| Blood creatinine increased                     | 242/229                      | NE [NE; NE]<br>13 (5.4)                                                                            | 240/235            | NE [NE; NE]<br>5 (2.1)                                                                             | 2.285 [0.811; 6.438]<br>0.1081                   |
| Lymphocyte count decreased                     | 242/232                      | NE [NE; NE]<br>10 (4.1)                                                                            | 240/234            | NE [NE; NE]<br>6 (2.5)                                                                             | 1.493 [0.540; 4.127]<br>0.4363                   |
| Neutrophil count decreased                     | 242/210                      | NE [NE; NE]<br>32 (13.2)                                                                           | 240/237            | NE [NE; NE]<br>3 (1.3)                                                                             | 9.989<br>[3.052; 32.687]<br><.0001               |

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

| Endpoint<br>SOC<br>PT                           | Lurbinectedin + atezolizumab |                                                                                                    | Atezolizumab       |                                                                                                    | Lurbinectedin + atezolizumab vs. atezolizumab    |
|-------------------------------------------------|------------------------------|----------------------------------------------------------------------------------------------------|--------------------|----------------------------------------------------------------------------------------------------|--------------------------------------------------|
|                                                 | N/N <sup>Cen</sup>           | Median time to event in days <sup>a</sup><br>[95% CI] <sup>b</sup><br>patients with event<br>n (%) | N/N <sup>Cen</sup> | Median time to event in days <sup>a</sup><br>[95% CI] <sup>b</sup><br>patients with event<br>n (%) | HR [95% CI] <sup>c</sup><br>p-value <sup>d</sup> |
| Platelet count decreased                        | 242/205                      | NE [NE; NE]<br>37 (15.3)                                                                           | 240/233            | NE [NE; NE]<br>7 (2.9)                                                                             | 5.174<br>[2.302; 11.632]<br><.0001               |
| White blood cell count decreased                | 242/223                      | NE [NE; NE]<br>19 (7.9)                                                                            | 240/235            | NE [NE; NE]<br>5 (2.1)                                                                             | 3.429 [1.276; 9.212]<br>0.0094                   |
| Metabolism and nutrition disorders              | 242/152                      | NE [359; NE]<br>90 (37.2)                                                                          | 240/182            | NE [466.000; NE]<br>58 (24.2)                                                                      | 1.589 [1.140; 2.215]<br>0.0058                   |
| Decreased appetite                              | 242/198                      | NE [NE; NE]<br>44 (18.2)                                                                           | 240/224            | NE [NE; NE]<br>16 (6.7)                                                                            | 2.745 [1.546; 4.872]<br>0.0003                   |
| Hypomagnesaemia                                 | 242/230                      | NE [NE; NE]<br>12 (5.0)                                                                            | 240/235            | NE [NE; NE]<br>5 (2.1)                                                                             | 2.312 [0.812; 6.582]<br>0.1060                   |
| Hyponatremia                                    | 242/231                      | NE [NE; NE]<br>11 (4.5)                                                                            | 240/225            | NE [NE; NE]<br>15 (6.3)                                                                            | 0.604 [0.276; 1.325]<br>0.2042                   |
| Musculoskeletal and connective tissue disorders | 242/183                      | NE [520; NE]<br>59 (24.4)                                                                          | 240/192            | NE [523.000; NE]<br>48 (20.0)                                                                      | 1.113 [0.758; 1.634]<br>0.5827                   |
| Arthralgia                                      | 242/222                      | NE [NE; NE]<br>20 (8.3)                                                                            | 240/228            | NE [NE; NE]<br>12 (5.0)                                                                            | 1.417 [0.690; 2.911]<br>0.3403                   |
| Back pain                                       | 242/228                      | NE [NE; NE]<br>14 (5.8)                                                                            | 240/230            | NE [NE; NE]<br>10 (4.2)                                                                            | 1.294 [0.573; 2.922]<br>0.5344                   |

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

| Endpoint<br>SOC<br>PT                           | Lurbinectedin + atezolizumab |                                                                                                    | Atezolizumab       |                                                                                                    | Lurbinectedin + atezolizumab vs. atezolizumab    |
|-------------------------------------------------|------------------------------|----------------------------------------------------------------------------------------------------|--------------------|----------------------------------------------------------------------------------------------------|--------------------------------------------------|
|                                                 | N/N <sup>Cen</sup>           | Median time to event in days <sup>a</sup><br>[95% CI] <sup>b</sup><br>patients with event<br>n (%) | N/N <sup>Cen</sup> | Median time to event in days <sup>a</sup><br>[95% CI] <sup>b</sup><br>patients with event<br>n (%) | HR [95% CI] <sup>c</sup><br>p-value <sup>d</sup> |
| Myalgia                                         | 242/230                      | NE [NE; NE]<br>12 (5.0)                                                                            | 240/236            | NE [NE; NE]<br>4 (1.7)                                                                             | 2.870 [0.924; 8.916]<br>0.0565                   |
| Nervous system disorders                        | 242/180                      | 630 [401; NE]<br>62 (25.6)                                                                         | 240/202            | NE [NE; NE]<br>38 (15.8)                                                                           | 1.393 [0.927; 2.091]<br>0.1088                   |
| Dizziness                                       | 242/223                      | NE [NE; NE]<br>19 (7.9)                                                                            | 240/235            | NE [NE; NE]<br>5 (2.1)                                                                             | 3.054 [1.134; 8.224]<br>0.0203                   |
| Headache                                        | 242/226                      | NE [NE; NE]<br>16 (6.6)                                                                            | 240/233            | NE [NE; NE]<br>7 (2.9)                                                                             | 1.890 [0.774; 4.619]<br>0.1556                   |
| Psychiatric disorders                           | 242/218                      | NE [NE; NE]<br>24 (9.9)                                                                            | 240/230            | NE [NE; NE]<br>10 (4.2)                                                                            | 1.989 [0.946; 4.181]<br>0.0643                   |
| Renal and urinary disorders                     | 242/224                      | NE [NE; NE]<br>18 (7.4)                                                                            | 240/230            | NE [NE; NE]<br>10 (4.2)                                                                            | 1.555 [0.714; 3.385]<br>0.2625                   |
| Respiratory, thoracic and mediastinal disorders | 242/165                      | NE [437; NE]<br>77 (31.8)                                                                          | 240/177            | 604.000 [441.000; NE]<br>63 (26.3)                                                                 | 1.134 [0.811; 1.585]<br>0.4596                   |
| Cough                                           | 242/218                      | NE [NE; NE]<br>24 (9.9)                                                                            | 240/223            | NE [NE; NE]<br>17 (7.1)                                                                            | 1.267 [0.679; 2.364]<br>0.4569                   |
| Dyspnea                                         | 242/216                      | NE [NE; NE]<br>26 (10.7)                                                                           | 240/220            | NE [NE; NE]<br>20 (8.3)                                                                            | 1.146 [0.637; 2.061]<br>0.6487                   |

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

| Endpoint<br>SOC<br>PT                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         | Lurbinectedin + atezolizumab |                                                                                                    | Atezolizumab       |                                                                                                    | Lurbinectedin + atezolizumab vs. atezolizumab    |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------|----------------------------------------------------------------------------------------------------|--------------------|----------------------------------------------------------------------------------------------------|--------------------------------------------------|
|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               | N/N <sup>Cen</sup>           | Median time to event in days <sup>a</sup><br>[95% CI] <sup>b</sup><br>patients with event<br>n (%) | N/N <sup>Cen</sup> | Median time to event in days <sup>a</sup><br>[95% CI] <sup>b</sup><br>patients with event<br>n (%) | HR [95% CI] <sup>c</sup><br>p-value <sup>d</sup> |
| Skin and subcutaneous tissue disorders                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        | 242/202                      | NE [NE; NE]<br>40 (16.5)                                                                           | 240/192            | NE [316.000; NE]<br>48 (20.0)                                                                      | 0.635 [0.414; 0.973]<br>0.0358                   |
| Pruritus                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | 242/223                      | NE [NE; NE]<br>19 (7.9)                                                                            | 240/221            | NE [NE; NE]<br>19 (7.9)                                                                            | 0.743 [0.389; 1.416]<br>0.3644                   |
| Vascular disorders                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            | 242/194                      | NE [545; NE]<br>48 (19.8)                                                                          | 240/227            | NE [NE; NE]<br>13 (5.4)                                                                            | 3.432 [1.856; 6.346]<br><.0001                   |
| Phlebitis                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | 242/225                      | NE [NE; NE]<br>17 (7.0)                                                                            | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE<br>[0.000; NE]<br><.0001                      |
| CCOD: 12 February 2025; NE: not estimable.<br>a: summaries of duration (median) are Kaplan-Meier estimates.<br>b: 95% CIs for the median were computed using the method of Brookmeyer and Crowley.<br>c: hazard ratios were estimated using a stratified Cox proportional hazard model. The stratification factors are ECOG PS at randomization (0 vs. 1), LDH at randomization ( $\leq$ ULN vs $>$ ULN) via local laboratory test, presence of liver metastases at enrollment (yes vs. no), and prior receipt of PCI (yes vs. no).<br>d: p-value based on the log rank test. |                              |                                                                                                    |                    |                                                                                                    |                                                  |

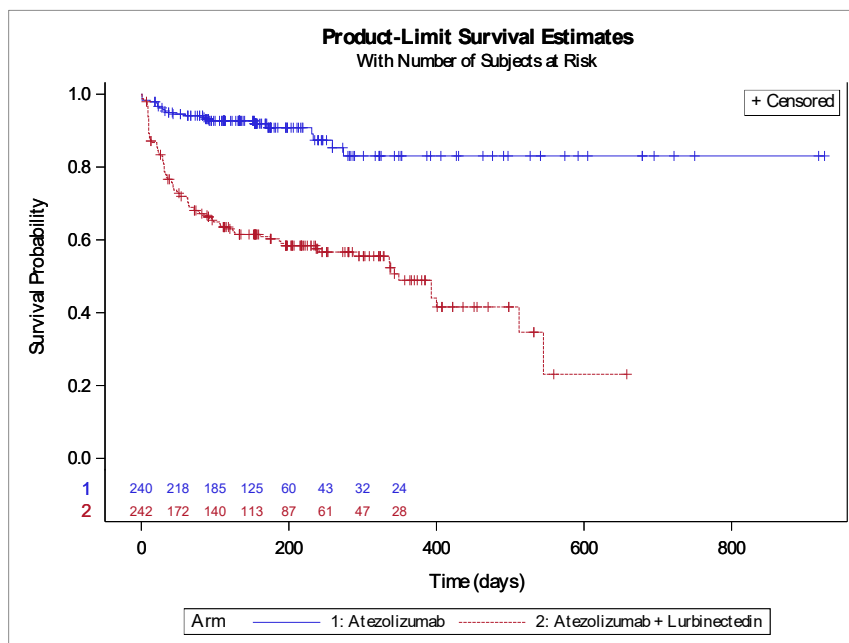


Abbildung 104: Kaplan-Meier plot for any AE (SOC blood and lymphatic system disorders), IMforte trial, Safety Analysis Set, CCOD 12 February 2025

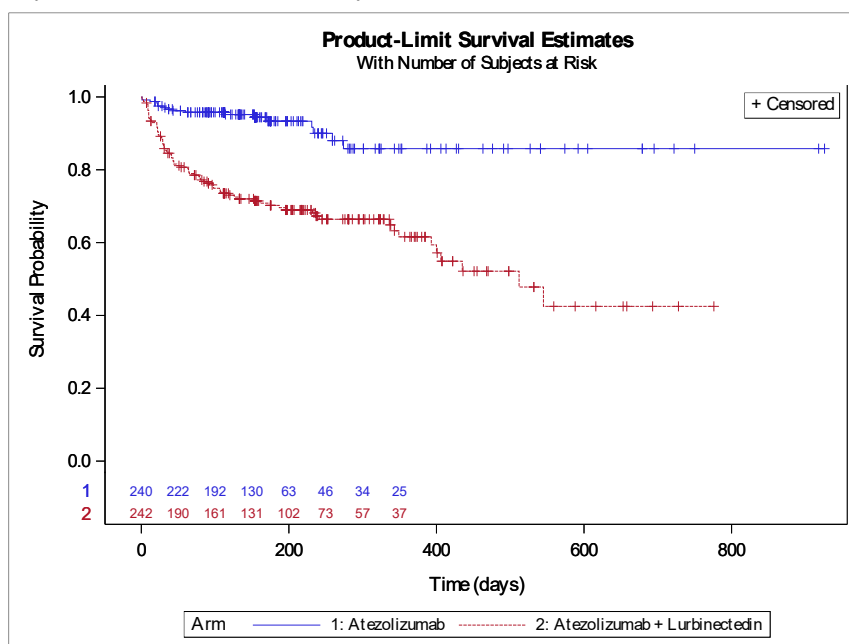


Abbildung 105: Kaplan-Meier plot for any AE (PT anemia), IMforte trial, Safety Analysis Set, CCOD 12 February 2025

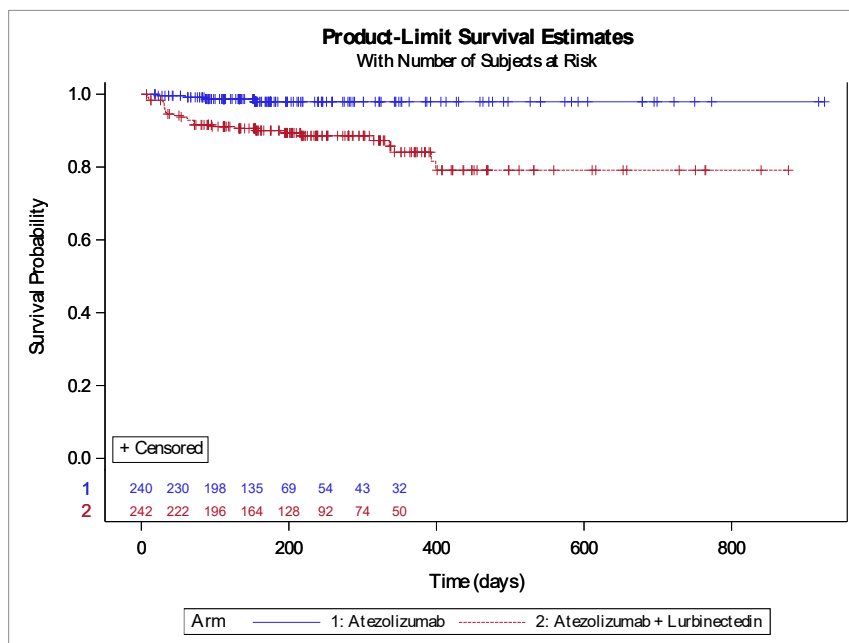


Abbildung 106: Kaplan-Meier plot for any AE (PT neutropenia), IMforte trial, Safety Analysis Set, CCOD 12 February 2025

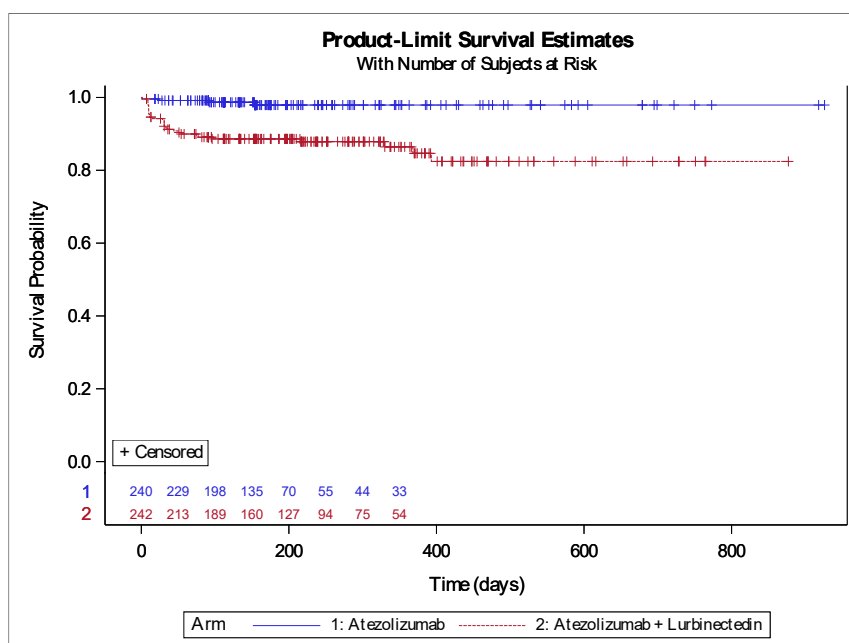


Abbildung 107: Kaplan-Meier plot for any AE (PT thrombocytopenia), IMforte trial, Safety Analysis Set, CCOD 12 February 2025

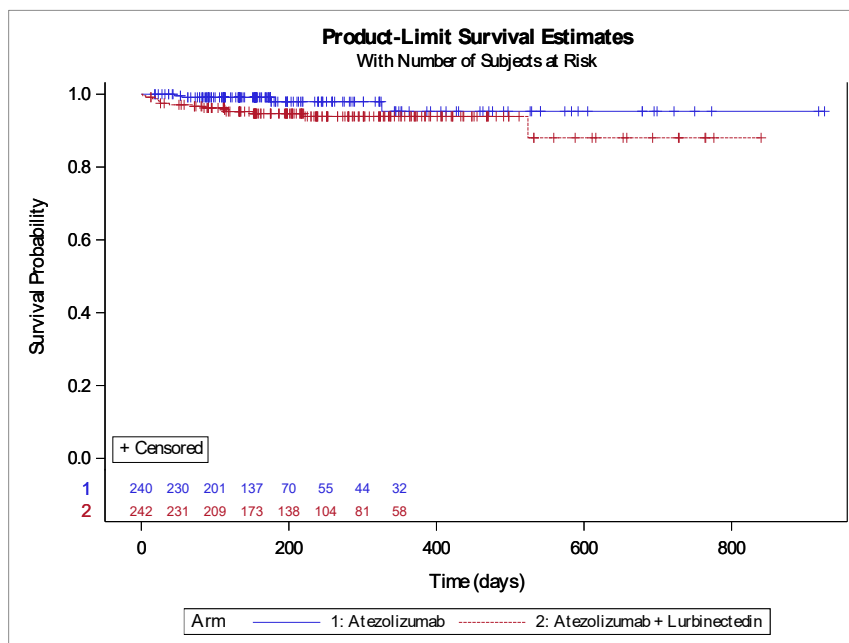


Abbildung 108: Kaplan-Meier plot for any AE (SOC cardiac disorders), IMforte trial, Safety Analysis Set, CCOD 12 February 2025

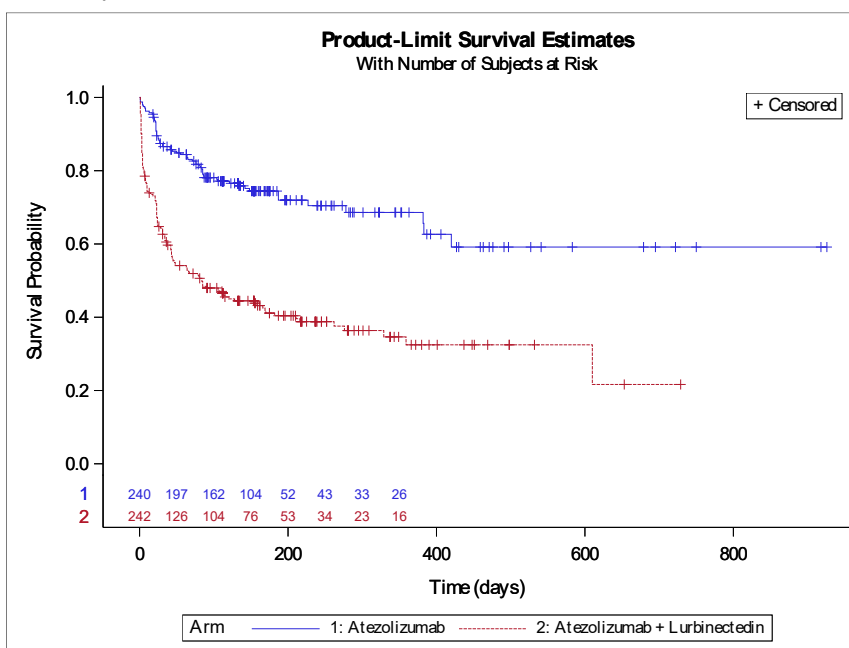


Abbildung 109: Kaplan-Meier plot for any AE (SOC gastrointestinal disorders), IMforte trial, Safety Analysis Set, CCOD 12 February 2025

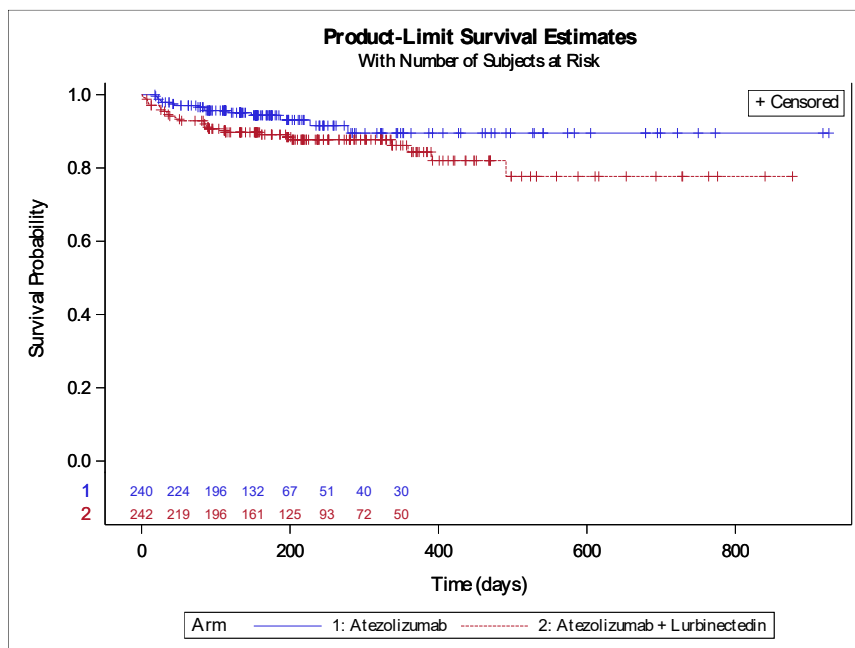


Abbildung 110: Kaplan-Meier plot for any AE (PT constipation), IMforte trial, Safety Analysis Set, CCOD 12 February 2025

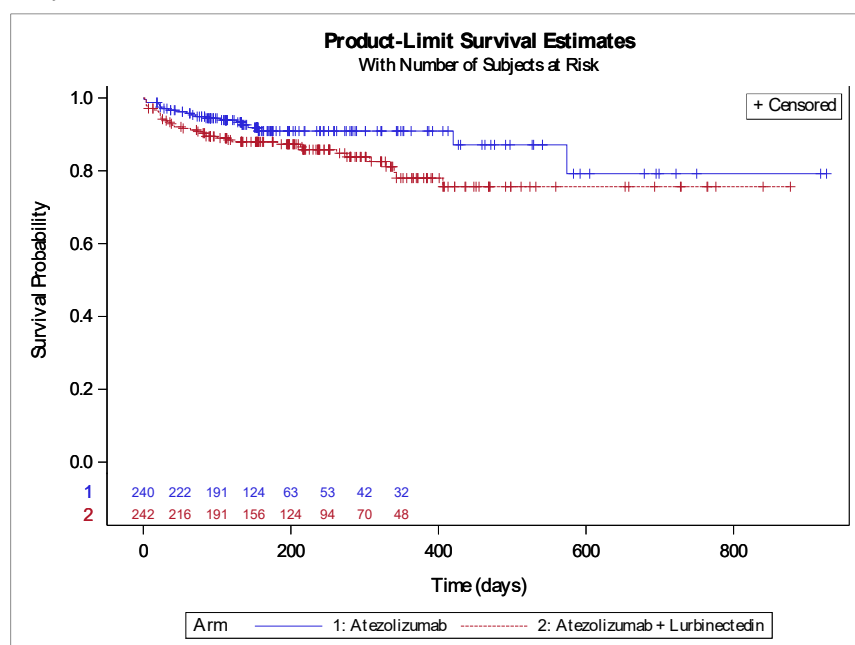


Abbildung 111: Kaplan-Meier plot for any AE (PT diarrhea), IMforte trial, Safety Analysis Set, CCOD 12 February 2025

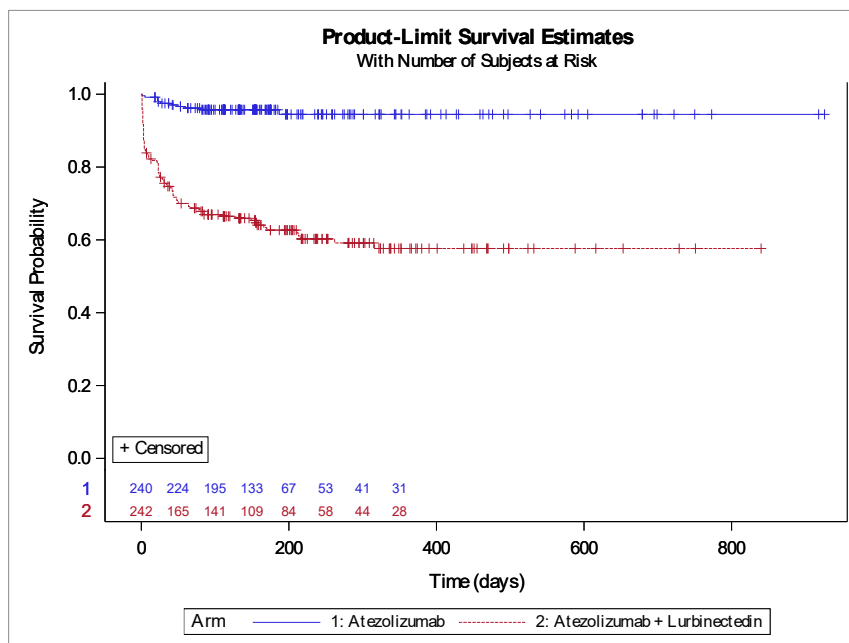


Abbildung 112: Kaplan-Meier plot for any AE (PT nausea), IMforte trial, Safety Analysis Set, CCOD 12 February 2025

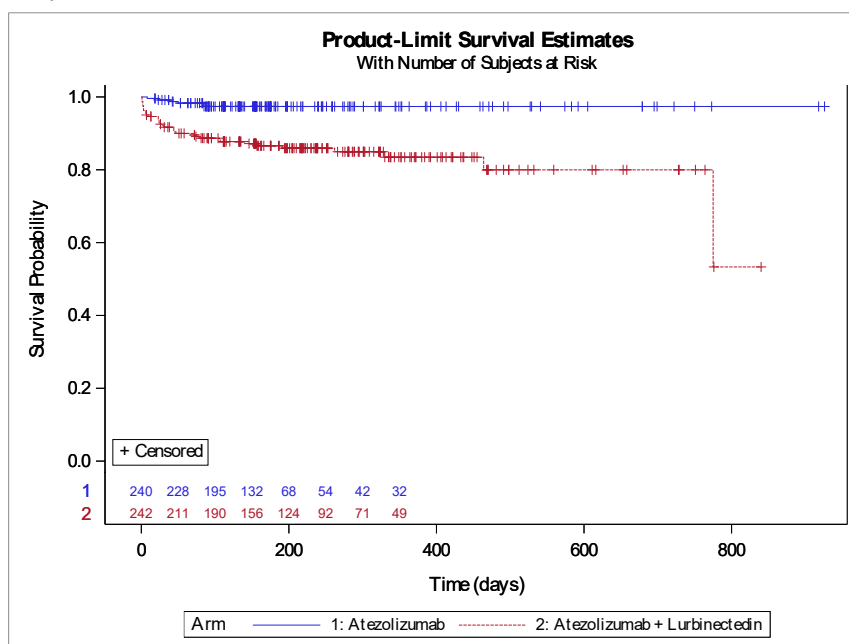


Abbildung 113: Kaplan-Meier plot for any AE (PT vomiting), IMforte trial, Safety Analysis Set, CCOD 12 February 2025

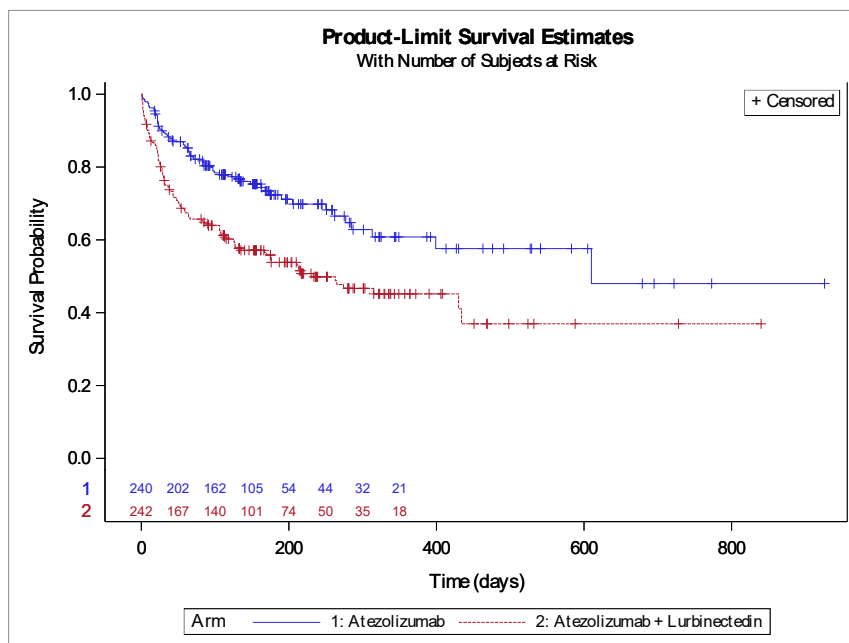


Abbildung 114: Kaplan-Meier plot for any AE (SOC general disorders and administration site conditions), IMforte trial, Safety Analysis Set, CCOD 12 February 2025

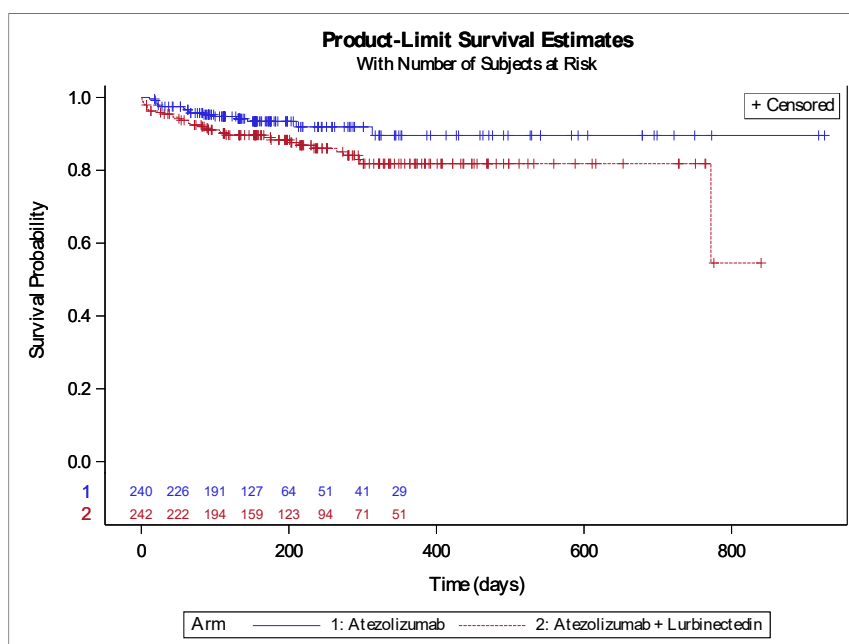


Abbildung 115: Kaplan-Meier plot for any AE (PT asthenia), IMforte trial, Safety Analysis Set, CCOD 12 February 2025

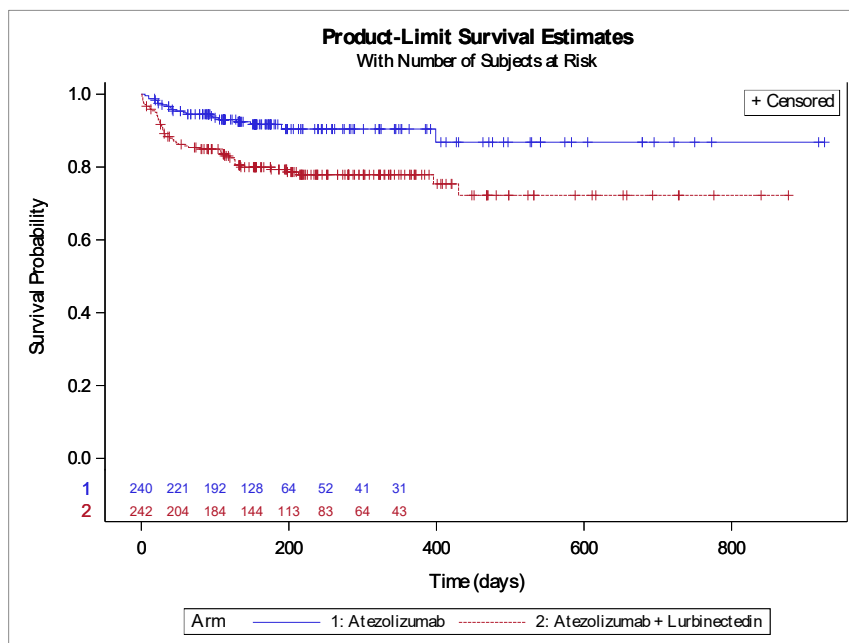


Abbildung 116: Kaplan-Meier plot for any AE (PT fatigue), IMforte trial, Safety Analysis Set, CCOD 12 February 2025

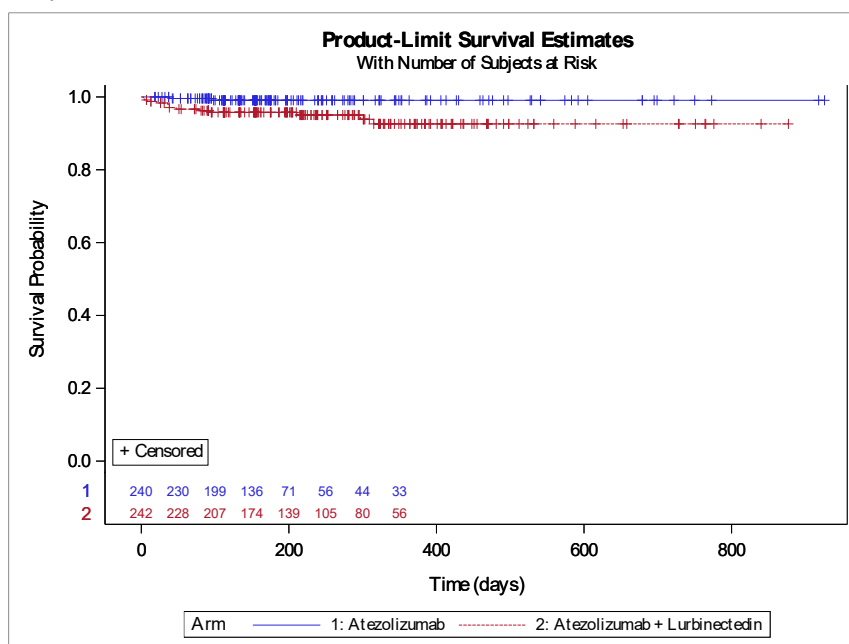


Abbildung 117: Kaplan-Meier plot for any AE (PT pyrexia), IMforte trial, Safety Analysis Set, CCOD 12 February 2025

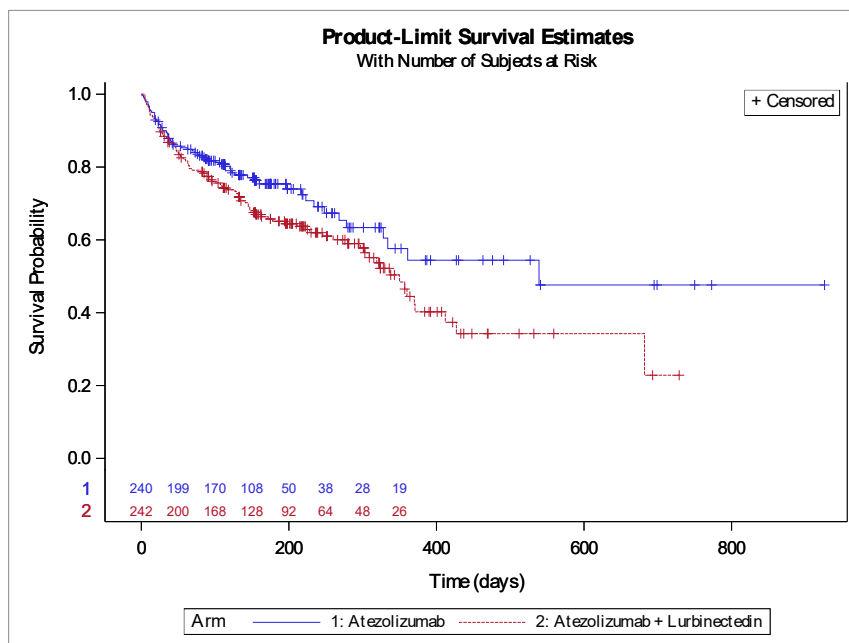


Abbildung 118: Kaplan-Meier plot for any AE (SOC infections and infestations), IMforte trial, Safety Analysis Set, CCOD 12 February 2025

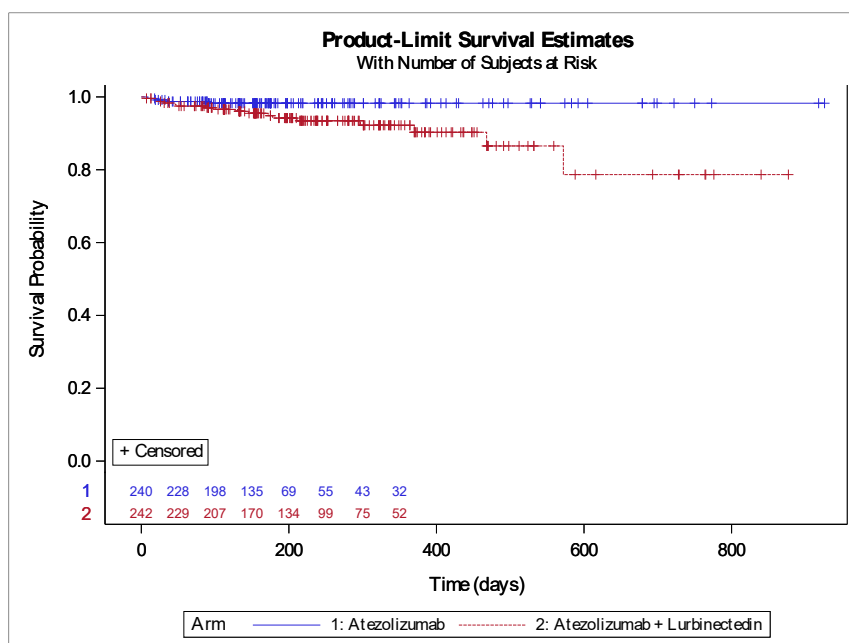


Abbildung 119: Kaplan-Meier plot for any AE (PT COVID-19), IMforte trial, Safety Analysis Set, CCOD 12 February 2025

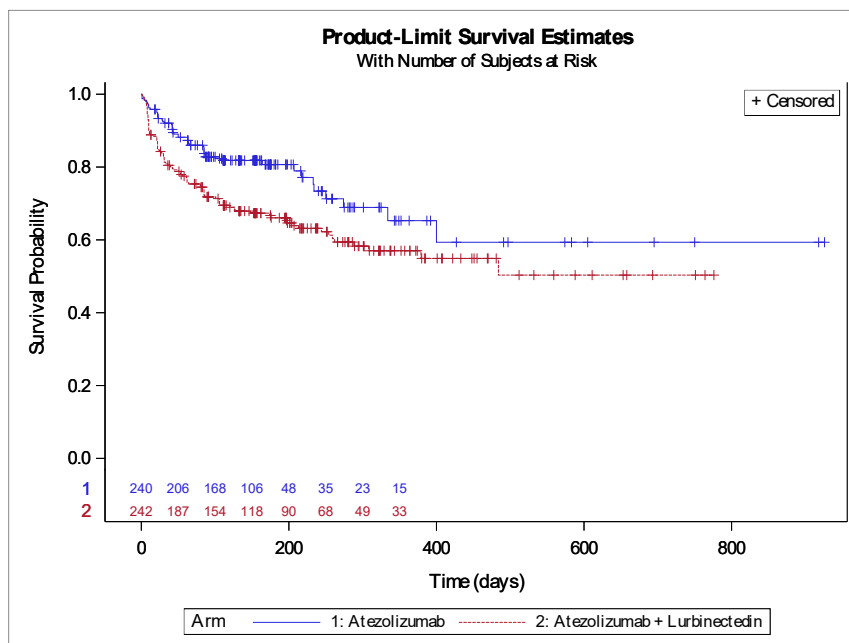


Abbildung 120: Kaplan-Meier plot for any AE (SOC investigations), IMforte trial, Safety Analysis Set, CCOD 12 February 2025

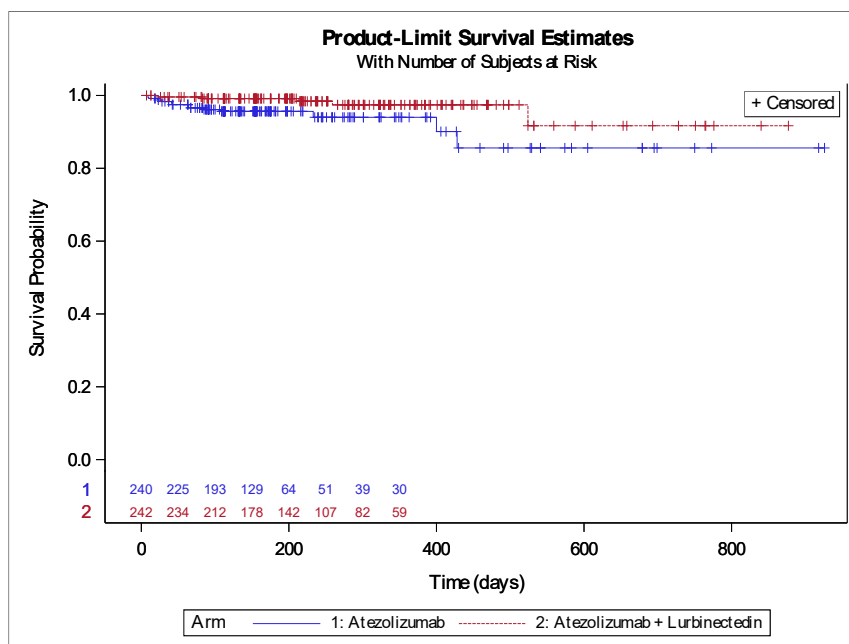


Abbildung 121: Kaplan-Meier plot for any AE (PT blood creatinine phosphokinase increased), IMforte trial, Safety Analysis Set, CCOD 12 February 2025

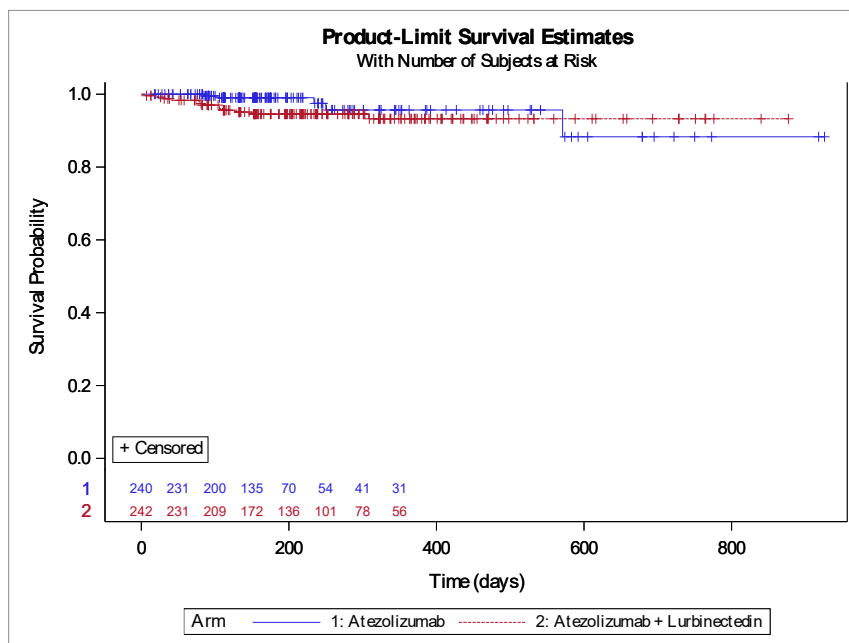


Abbildung 122: Kaplan-Meier plot for any AE (PT blood creatinine increased), IMforte trial, Safety Analysis Set, CCOD 12 February 2025

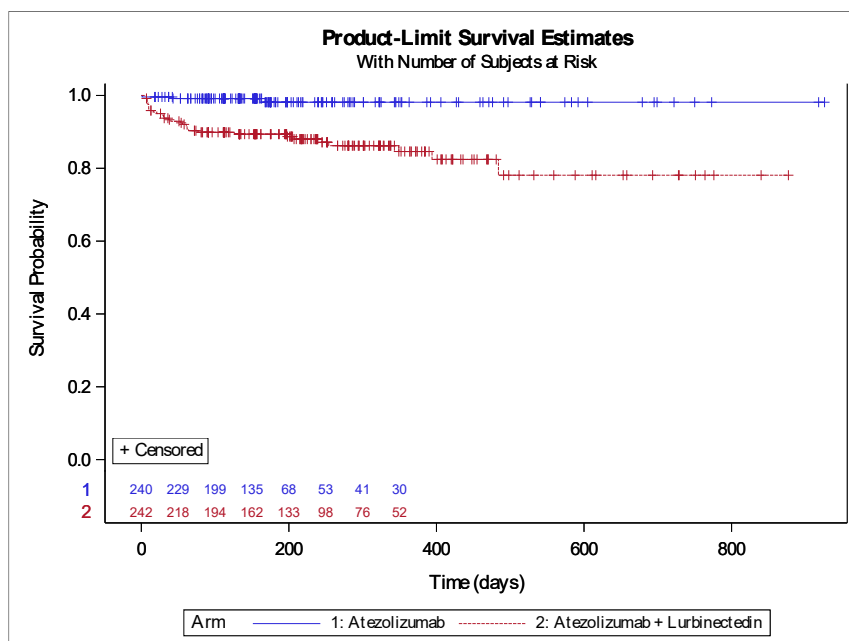


Abbildung 123: Kaplan-Meier plot for any AE (PT neutrophil count decreased), IMforte trial, Safety Analysis Set, CCOD 12 February 2025

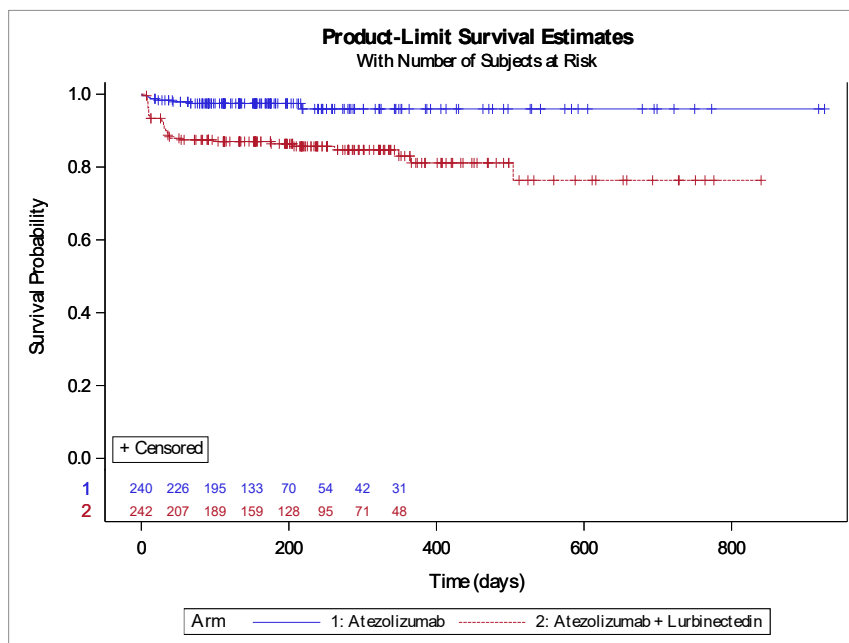


Abbildung 124: Kaplan-Meier plot for any AE (PT platelet count decreased), IMforte trial, Safety Analysis Set, CCOD 12 February 2025

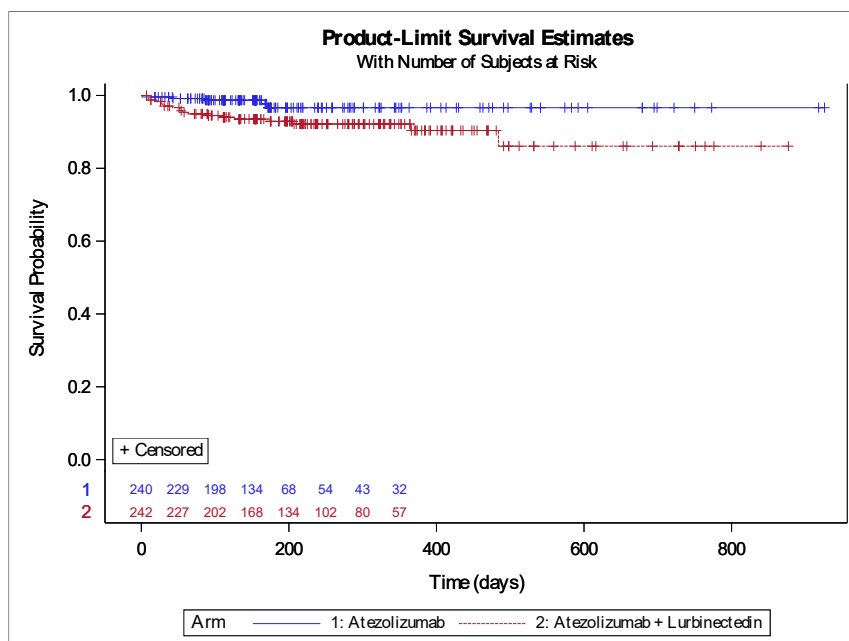


Abbildung 125: Kaplan-Meier plot for any AE (PT white blood cell count decreased), IMforte trial, Safety Analysis Set, CCOD 12 February 2025

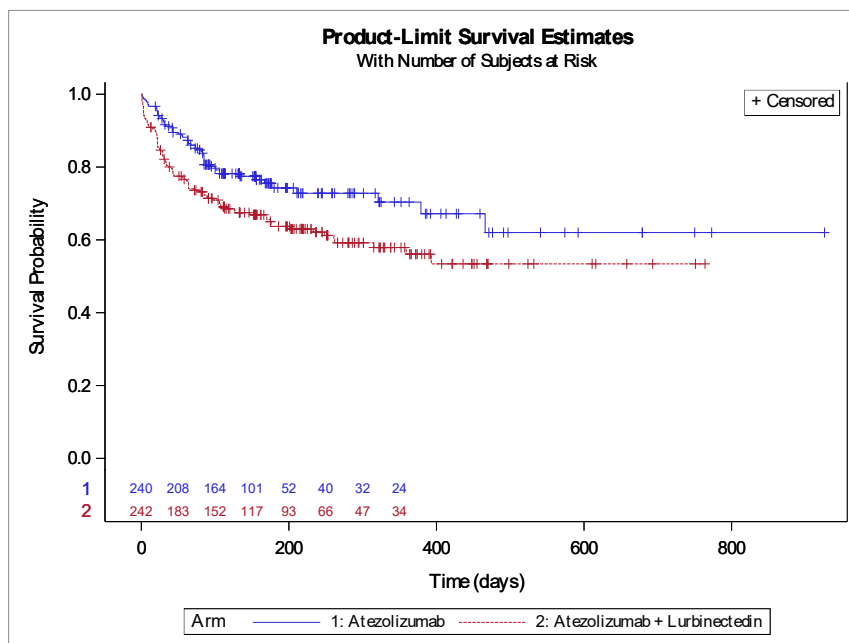


Abbildung 126: Kaplan-Meier plot for any AE (SOC metabolism and nutrition disorders), IMforte trial, Safety Analysis Set, CCOD 12 February 2025

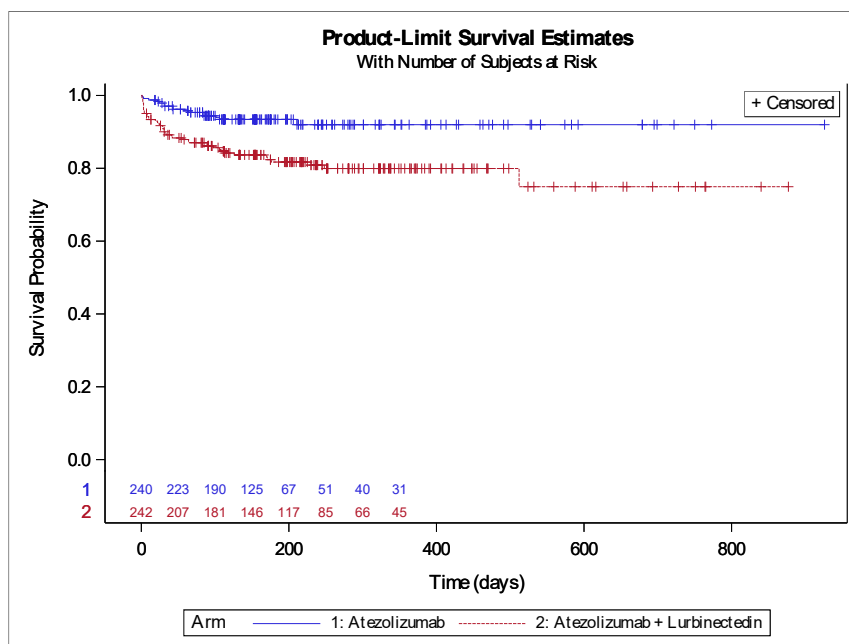


Abbildung 127: Kaplan-Meier plot for any AE (PT decreased appetite), IMforte trial, Safety Analysis Set, CCOD 12 February 2025

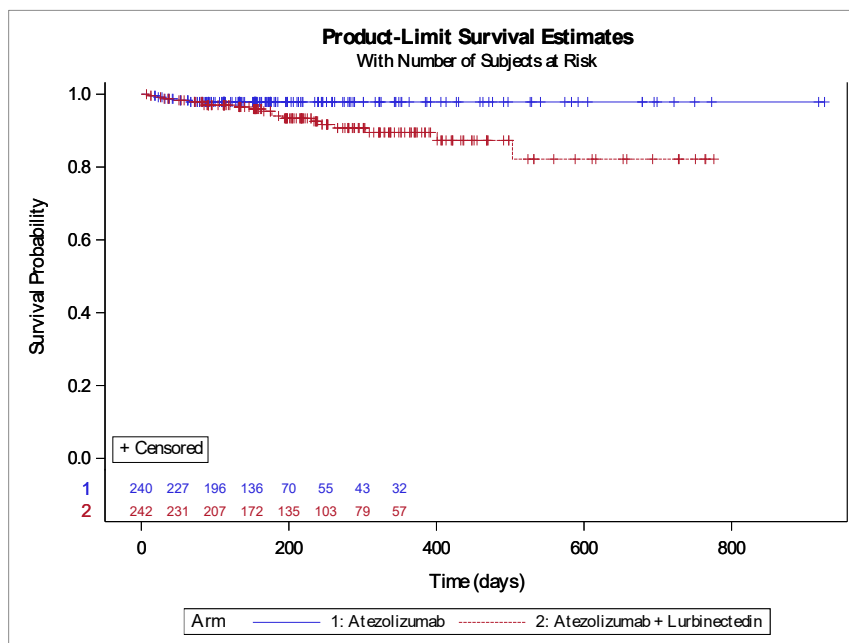


Abbildung 128: Kaplan-Meier plot for any AE (PT dizziness), IMforte trial, Safety Analysis Set, CCOD 12 February 2025

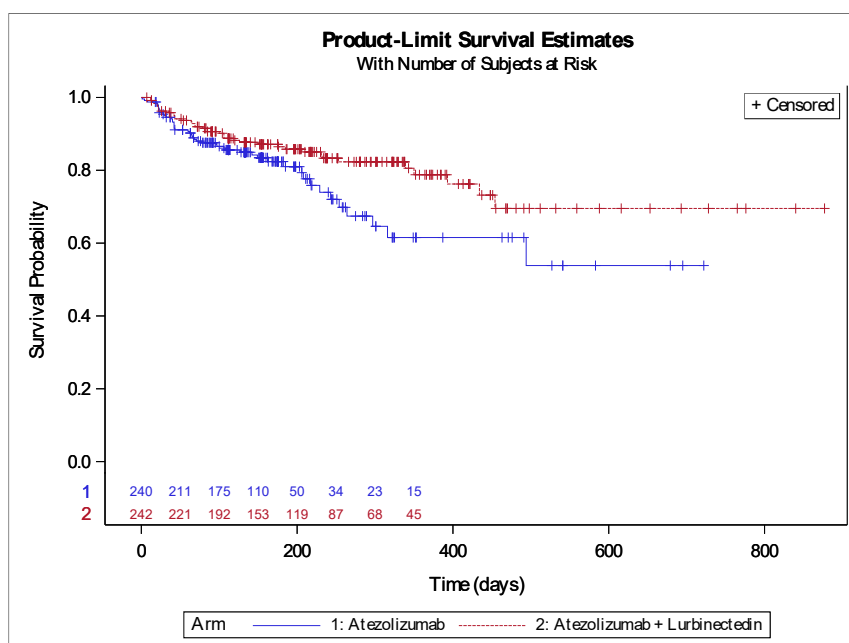


Abbildung 129: Kaplan-Meier plot for any AE (SOC skin and subcutaneous tissue disorders), IMforte trial, Safety Analysis Set, CCOD 12 February 2025

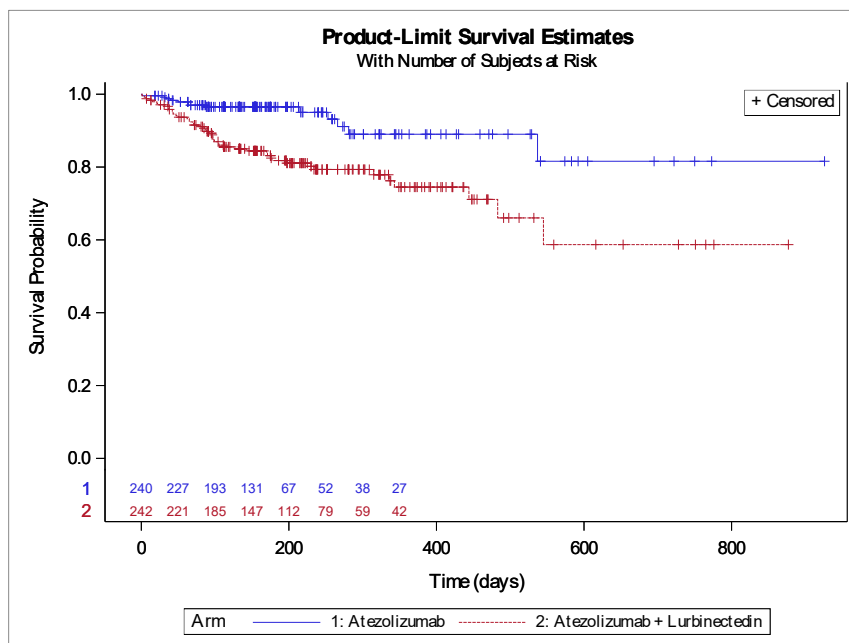


Abbildung 130: Kaplan-Meier plot for any AE (SOC vascular disorders), IMforte trial, Safety Analysis Set, CCOD 12 February 2025

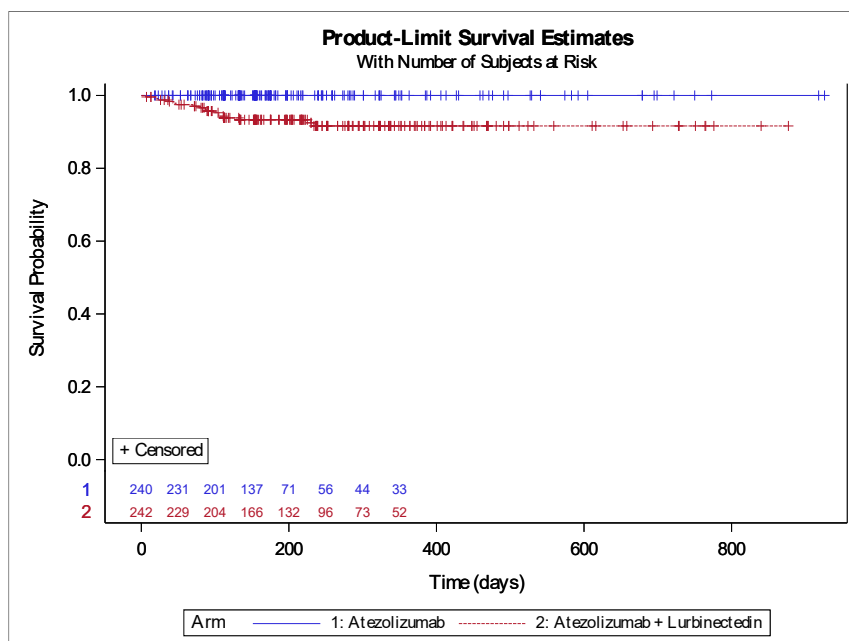


Abbildung 131: Kaplan-Meier plot for any AE (PT phlebitis), IMforte trial, Safety Analysis Set, CCOD 12 February 2025

Tabelle 11: Severe AE (CTCAE  $\geq 3$ ) by SOC and PT including effect estimates

| Endpoint<br>SOC<br>PT                | Lurbinectedin + atezolizumab |                                                                                                       | Atezolizumab       |                                                                                                    | Lurbinectedin + atezolizumab vs.<br>atezolizumab |
|--------------------------------------|------------------------------|-------------------------------------------------------------------------------------------------------|--------------------|----------------------------------------------------------------------------------------------------|--------------------------------------------------|
|                                      | N/N <sup>Cen</sup>           | Median time to event in<br>days <sup>a</sup><br>[95% CI] <sup>b</sup><br>patients with event<br>n (%) | N/N <sup>Cen</sup> | Median time to event in days <sup>a</sup><br>[95% CI] <sup>b</sup><br>patients with event<br>n (%) | HR [95% CI] <sup>c</sup><br>p-value <sup>d</sup> |
| Blood and lymphatic system disorders | 242/199                      | NE [545; NE]<br>43 (17.8)                                                                             | 240/236            | NE [NE; NE]<br>4 (1.7)                                                                             | 10.345 [3.707; 28.864]<br><.0001                 |
| Anemia                               | 242/219                      | NE [NE; NE]<br>23 (9.5)                                                                               | 240/238            | NE [NE; NE]<br>2 (0.8)                                                                             | 10.512 [2.474; 44.669]<br><.0001                 |
| Febrile neutropenia                  | 242/238                      | NE [NE; NE]<br>4 (1.7)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [0.000; NE]<br>0.0504                         |
| Leukocytosis                         | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [0.000; NE]<br>0.3237                         |
| Leukopenia                           | 242/240                      | NE [NE; NE]<br>2 (0.8)                                                                                | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                             | 1.814 [0.164; 20.103]<br>0.6223                  |
| Lymphadenitis                        | 242/242                      | NE [NE; NE]<br>0 (0.0)                                                                                | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                             | 0.000 [0.000; NE]<br>0.3153                      |
| Lymphopenia                          | 242/239                      | NE [NE; NE]<br>3 (1.2)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [0.000; NE]<br>0.1169                         |
| Neutropenia                          | 242/230                      | NE [NE; NE]<br>12 (5.0)                                                                               | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                             | 11.006 [1.428; 84.838]<br>0.0039                 |

| Endpoint<br>SOC<br>PT          | Lurbinectedin + atezolizumab |                                                                                                       | Atezolizumab       |                                                                                                    | Lurbinectedin + atezolizumab vs.<br>atezolizumab |
|--------------------------------|------------------------------|-------------------------------------------------------------------------------------------------------|--------------------|----------------------------------------------------------------------------------------------------|--------------------------------------------------|
|                                | N/N <sup>Cen</sup>           | Median time to event in<br>days <sup>a</sup><br>[95% CI] <sup>b</sup><br>patients with event<br>n (%) | N/N <sup>Cen</sup> | Median time to event in days <sup>a</sup><br>[95% CI] <sup>b</sup><br>patients with event<br>n (%) | HR [95% CI] <sup>c</sup><br>p-value <sup>d</sup> |
| Pancytopenia                   | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [0.000; NE]<br>0.4540                         |
| Thrombocytopenia               | 242/231                      | NE [NE; NE]<br>11 (4.5)                                                                               | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                             | 10.049 [1.294; 78.020]<br>0.0065                 |
| Cardiac disorders              | 242/234                      | NE [NE; NE]<br>8 (3.3)                                                                                | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                             | 6.911 [0.860; 55.549]<br>0.0350                  |
| Acute myocardial<br>infarction | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [0.000; NE]<br>0.3574                         |
| Atrial fibrillation            | 242/240                      | NE [NE; NE]<br>2 (0.8)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [0.000; NE]<br>0.1569                         |
| Cardio-<br>respiratory arrest  | 242/240                      | NE [NE; NE]<br>2 (0.8)                                                                                | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                             | 1.608 [0.143; 18.122]<br>0.6980                  |
| Myocardial<br>infarction       | 242/239                      | NE [NE; NE]<br>3 (1.2)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [0.000; NE]<br>0.1201                         |
| Ear and labyrinth<br>disorders | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [0.000; NE]<br>0.3215                         |
| Vertigo                        | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [0.000; NE]<br>0.3215                         |

| Endpoint<br>SOC<br>PT          | Lurbinectedin + atezolizumab |                                                                                                       | Atezolizumab       |                                                                                                    | Lurbinectedin + atezolizumab vs.<br>atezolizumab |
|--------------------------------|------------------------------|-------------------------------------------------------------------------------------------------------|--------------------|----------------------------------------------------------------------------------------------------|--------------------------------------------------|
|                                | N/N <sup>Cen</sup>           | Median time to event in<br>days <sup>a</sup><br>[95% CI] <sup>b</sup><br>patients with event<br>n (%) | N/N <sup>Cen</sup> | Median time to event in days <sup>a</sup><br>[95% CI] <sup>b</sup><br>patients with event<br>n (%) | HR [95% CI] <sup>c</sup><br>p-value <sup>d</sup> |
| Endocrine disorders            | 242/242                      | NE [NE; NE]<br>0 (0.0)                                                                                | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                             | 0.000 [0.000; NE]<br>0.3131                      |
| Adrenal<br>insufficiency       | 242/242                      | NE [NE; NE]<br>0 (0.0)                                                                                | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                             | 0.000 [0.000; NE]<br>0.3131                      |
| Gastrointestinal<br>disorders  | 242/231                      | NE [NE; NE]<br>11 (4.5)                                                                               | 240/232            | NE [NE; NE]<br>8 (3.3)                                                                             | 1.256 [0.503; 3.136]<br>0.6244                   |
| Abdominal pain                 | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [0.000; NE]<br>0.4348                         |
| Chronic gastritis              | 242/242                      | NE [NE; NE]<br>0 (0.0)                                                                                | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                             | 0.000 [0.000; NE]<br>0.2123                      |
| Constipation                   | 242/242                      | NE [NE; NE]<br>0 (0.0)                                                                                | 240/238            | NE [NE; NE]<br>2 (0.8)                                                                             | 0.000 [0.000; NE]<br>0.1527                      |
| Diarrhea                       | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                             | 0.701 [0.042; 11.680]<br>0.8033                  |
| Gastrointestinal<br>hemorrhage | 242/242                      | NE [NE; NE]<br>0 (0.0)                                                                                | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                             | 0.000 [0.000; NE]<br>0.3110                      |
| Ileus                          | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [0.000; NE]<br>0.3193                         |

| Endpoint<br>SOC<br>PT                                      | Lurbinectedin + atezolizumab |                                                                                                       | Atezolizumab       |                                                                                                    | Lurbinectedin + atezolizumab vs.<br>atezolizumab |
|------------------------------------------------------------|------------------------------|-------------------------------------------------------------------------------------------------------|--------------------|----------------------------------------------------------------------------------------------------|--------------------------------------------------|
|                                                            | N/N <sup>Cen</sup>           | Median time to event in<br>days <sup>a</sup><br>[95% CI] <sup>b</sup><br>patients with event<br>n (%) | N/N <sup>Cen</sup> | Median time to event in days <sup>a</sup><br>[95% CI] <sup>b</sup><br>patients with event<br>n (%) | HR [95% CI] <sup>c</sup><br>p-value <sup>d</sup> |
| Nausea                                                     | 242/235                      | NE [NE; NE]<br>7 (2.9)                                                                                | 240/238            | NE [NE; NE]<br>2 (0.8)                                                                             | 3.497 [0.726; 16.838]<br>0.0959                  |
| Pancreatitis acute                                         | 242/242                      | NE [NE; NE]<br>0 (0.0)                                                                                | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                             | 0.000 [0.000; NE]<br>0.3152                      |
| Pancreatitis<br>chronic                                    | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [0.000; NE]<br>0.3325                         |
| Volvulus                                                   | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                             | 0.735 [0.045; 12.100]<br>0.8288                  |
| Vomiting                                                   | 242/240                      | NE [NE; NE]<br>2 (0.8)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [0.000; NE]<br>0.1609                         |
| General disorders<br>and administration<br>site conditions | 242/226                      | NE [NE; NE]<br>16 (6.6)                                                                               | 240/231            | NE [NE; NE]<br>9 (3.8)                                                                             | 1.481 [0.651; 3.374]<br>0.3463                   |
| Adhesion                                                   | 242/242                      | NE [NE; NE]<br>0 (0.0)                                                                                | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                             | 0.000 [0.000; NE]<br>0.1613                      |
| Asthenia                                                   | 242/239                      | NE [NE; NE]<br>3 (1.2)                                                                                | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                             | 2.273 [0.233; 22.211]<br>0.4685                  |
| Chest pain                                                 | 242/242                      | NE [NE; NE]<br>0 (0.0)                                                                                | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                             | 0.000 [0.000; NE]<br>0.1596                      |

| Endpoint<br>SOC<br>PT                       | Lurbinectedin + atezolizumab |                                                                                                       | Atezolizumab       |                                                                                                    | Lurbinectedin + atezolizumab vs.<br>atezolizumab |
|---------------------------------------------|------------------------------|-------------------------------------------------------------------------------------------------------|--------------------|----------------------------------------------------------------------------------------------------|--------------------------------------------------|
|                                             | N/N <sup>Cen</sup>           | Median time to event in<br>days <sup>a</sup><br>[95% CI] <sup>b</sup><br>patients with event<br>n (%) | N/N <sup>Cen</sup> | Median time to event in days <sup>a</sup><br>[95% CI] <sup>b</sup><br>patients with event<br>n (%) | HR [95% CI] <sup>c</sup><br>p-value <sup>d</sup> |
| Death                                       | 242/242                      | NE [NE; NE]<br>0 (0.0)                                                                                | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                             | 0.000 [0.000; NE]<br>0.1886                      |
| Fatigue                                     | 242/233                      | NE [NE; NE]<br>9 (3.7)                                                                                | 240/237            | NE [NE; NE]<br>3 (1.3)                                                                             | 2.872 [0.776; 10.623]<br>0.0981                  |
| Gait disturbance                            | 242/242                      | NE [NE; NE]<br>0 (0.0)                                                                                | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                             | 0.000 [0.000; NE]<br>0.1588                      |
| General physical<br>health<br>deterioration | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [0.000; NE]<br>0.3204                         |
| Influenza like<br>illness                   | 242/242                      | NE [NE; NE]<br>0 (0.0)                                                                                | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                             | 0.000 [0.000; NE]<br>0.3153                      |
| Oedema<br>peripheral                        | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [0.000; NE]<br>0.4752                         |
| Pain                                        | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [0.000; NE]<br>0.3205                         |
| Peripheral<br>swelling                      | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [0.000; NE]<br>0.3205                         |
| Hepatobiliary<br>disorders                  | 242/239                      | NE [NE; NE]<br>3 (1.2)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [0.000; NE]<br>0.1171                         |

| Endpoint<br>SOC<br>PT       | Lurbinectedin + atezolizumab |                                                                                                       | Atezolizumab       |                                                                                                    | Lurbinectedin + atezolizumab vs.<br>atezolizumab |
|-----------------------------|------------------------------|-------------------------------------------------------------------------------------------------------|--------------------|----------------------------------------------------------------------------------------------------|--------------------------------------------------|
|                             | N/N <sup>Cen</sup>           | Median time to event in<br>days <sup>a</sup><br>[95% CI] <sup>b</sup><br>patients with event<br>n (%) | N/N <sup>Cen</sup> | Median time to event in days <sup>a</sup><br>[95% CI] <sup>b</sup><br>patients with event<br>n (%) | HR [95% CI] <sup>c</sup><br>p-value <sup>d</sup> |
| Cholecystitis               | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [0.000; NE]<br>0.3237                         |
| Cholestasis                 | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [0.000; NE]<br>0.4677                         |
| Immune-mediated hepatitis   | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [0.000; NE]<br>0.3237                         |
| Infections and infestations | 242/219                      | NE [NE; NE]<br>23 (9.5)                                                                               | 240/224            | NE [NE; NE]<br>16 (6.7)                                                                            | 1.240 [0.652; 2.357]<br>0.5109                   |
| Abscess intestinal          | 242/242                      | NE [NE; NE]<br>0 (0.0)                                                                                | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                             | 0.000 [0.000; NE]<br>0.3183                      |
| COVID-19                    | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                             | 0.985 [0.062; 15.750]<br>0.9915                  |
| COVID-19 pneumonia          | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [0.000; NE]<br>0.3193                         |
| Cellulitis                  | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [0.000; NE]<br>0.3204                         |
| Encephalitis                | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                             | 0.860 [0.054; 13.744]<br>0.9148                  |

| Endpoint<br>SOC<br>PT                  | Lurbinectedin + atezolizumab |                                                                                                       | Atezolizumab       |                                                                                                    | Lurbinectedin + atezolizumab vs.<br>atezolizumab |
|----------------------------------------|------------------------------|-------------------------------------------------------------------------------------------------------|--------------------|----------------------------------------------------------------------------------------------------|--------------------------------------------------|
|                                        | N/N <sup>Cen</sup>           | Median time to event in<br>days <sup>a</sup><br>[95% CI] <sup>b</sup><br>patients with event<br>n (%) | N/N <sup>Cen</sup> | Median time to event in days <sup>a</sup><br>[95% CI] <sup>b</sup><br>patients with event<br>n (%) | HR [95% CI] <sup>c</sup><br>p-value <sup>d</sup> |
| Infection                              | 242/239                      | NE [NE; NE]<br>3 (1.2)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [0.000; NE]<br>0.0839                         |
| Lower respiratory<br>tract infection   | 242/240                      | NE [NE; NE]<br>2 (0.8)                                                                                | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                             | 1.963 [0.178; 21.643]<br>0.5747                  |
| Pharyngitis                            | 242/242                      | NE [NE; NE]<br>0 (0.0)                                                                                | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                             | 0.000 [0.000; NE]<br>0.2768                      |
| Pneumocystis<br>jirovecii<br>pneumonia | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [0.000; NE]<br>0.3183                         |
| Pneumonia                              | 242/235                      | NE [NE; NE]<br>7 (2.9)                                                                                | 240/234            | NE [NE; NE]<br>6 (2.5)                                                                             | 0.964 [0.321; 2.898]<br>0.9487                   |
| Pneumonia viral                        | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [0.000; NE]<br>0.3193                         |
| Pyelonephritis<br>acute                | 242/242                      | NE [NE; NE]<br>0 (0.0)                                                                                | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                             | 0.000 [0.000; NE]<br>0.3152                      |
| Respiratory tract<br>infection         | 242/238                      | NE [NE; NE]<br>4 (1.7)                                                                                | 240/238            | NE [NE; NE]<br>2 (0.8)                                                                             | 1.511 [0.273; 8.354]<br>0.6337                   |
| Sepsis                                 | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                             | 0.711 [0.043; 11.771]<br>0.8112                  |

| Endpoint<br>SOC<br>PT                          | Lurbinectedin + atezolizumab |                                                                                                       | Atezolizumab       |                                                                                                    | Lurbinectedin + atezolizumab vs.<br>atezolizumab |
|------------------------------------------------|------------------------------|-------------------------------------------------------------------------------------------------------|--------------------|----------------------------------------------------------------------------------------------------|--------------------------------------------------|
|                                                | N/N <sup>Cen</sup>           | Median time to event in<br>days <sup>a</sup><br>[95% CI] <sup>b</sup><br>patients with event<br>n (%) | N/N <sup>Cen</sup> | Median time to event in days <sup>a</sup><br>[95% CI] <sup>b</sup><br>patients with event<br>n (%) | HR [95% CI] <sup>c</sup><br>p-value <sup>d</sup> |
| Urinary tract infection                        | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                             | 0.863 [0.054; 13.872]<br>0.9168                  |
| Urosepsis                                      | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [0.000; NE]<br>0.3237                         |
| Vascular device infection                      | 242/240                      | NE [NE; NE]<br>2 (0.8)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [0.000; NE]<br>0.2258                         |
| Injury, poisoning and procedural complications | 242/240                      | NE [NE; NE]<br>2 (0.8)                                                                                | 240/238            | NE [NE; NE]<br>2 (0.8)                                                                             | 0.753 [0.104; 5.445]<br>0.7777                   |
| Ankle fracture                                 | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [0.000; NE]<br>0.4781                         |
| Femur fracture                                 | 242/242                      | NE [NE; NE]<br>0 (0.0)                                                                                | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                             | 0.000 [0.000; NE]<br>0.3153                      |
| Hip fracture                                   | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [0.000; NE]<br>0.3966                         |
| Humerus fracture                               | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [0.000; NE]<br>0.3545                         |
| Road traffic accident                          | 242/242                      | NE [NE; NE]<br>0 (0.0)                                                                                | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                             | 0.000 [0.000; NE]<br>0.3047                      |

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

| Endpoint<br>SOC<br>PT                        | Lurbinectedin + atezolizumab |                                                                                                       | Atezolizumab       |                                                                                                    | Lurbinectedin + atezolizumab vs.<br>atezolizumab |
|----------------------------------------------|------------------------------|-------------------------------------------------------------------------------------------------------|--------------------|----------------------------------------------------------------------------------------------------|--------------------------------------------------|
|                                              | N/N <sup>Cen</sup>           | Median time to event in<br>days <sup>a</sup><br>[95% CI] <sup>b</sup><br>patients with event<br>n (%) | N/N <sup>Cen</sup> | Median time to event in days <sup>a</sup><br>[95% CI] <sup>b</sup><br>patients with event<br>n (%) | HR [95% CI] <sup>c</sup><br>p-value <sup>d</sup> |
| Investigations                               | 242/212                      | NE [NE; NE]<br>30 (12.4)                                                                              | 240/228            | NE [NE; NE]<br>12 (5.0)                                                                            | 2.366 [1.208; 4.635]<br>0.0097                   |
| Alanine<br>aminotransferase<br>increased     | 242/236                      | NE [NE; NE]<br>6 (2.5)                                                                                | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                             | 5.630 [0.677; 46.861]<br>0.0713                  |
| Aspartate<br>aminotransferase<br>increased   | 242/239                      | NE [NE; NE]<br>3 (1.2)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [0.000; NE]<br>0.0844                         |
| Blood alkaline<br>phosphatase<br>increased   | 242/242                      | NE [NE; NE]<br>0 (0.0)                                                                                | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                             | 0.000 [0.000; NE]<br>0.3132                      |
| Blood bilirubin<br>increased                 | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [0.000; NE]<br>0.3258                         |
| Blood creatine<br>phosphokinase<br>increased | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/238            | NE [NE; NE]<br>2 (0.8)                                                                             | 0.482 [0.044; 5.320]<br>0.5429                   |
| Ejection fraction<br>decreased               | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [0.000; NE]<br>0.3183                         |
| Gamma-<br>glutamyltrans-<br>ferase increased | 242/240                      | NE [NE; NE]<br>2 (0.8)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [0.000; NE]<br>0.1591                         |
| Lipase increased                             | 242/242                      | NE [NE; NE]<br>0 (0.0)                                                                                | 240/238            | NE [NE; NE]<br>2 (0.8)                                                                             | 0.000 [0.000; NE]<br>0.1522                      |

| Endpoint<br>SOC<br>PT                    | Lurbinectedin + atezolizumab |                                                                                                       | Atezolizumab       |                                                                                                    | Lurbinectedin + atezolizumab vs.<br>atezolizumab |
|------------------------------------------|------------------------------|-------------------------------------------------------------------------------------------------------|--------------------|----------------------------------------------------------------------------------------------------|--------------------------------------------------|
|                                          | N/N <sup>Cen</sup>           | Median time to event in<br>days <sup>a</sup><br>[95% CI] <sup>b</sup><br>patients with event<br>n (%) | N/N <sup>Cen</sup> | Median time to event in days <sup>a</sup><br>[95% CI] <sup>b</sup><br>patients with event<br>n (%) | HR [95% CI] <sup>c</sup><br>p-value <sup>d</sup> |
| Liver function<br>test increased         | 242/242                      | NE [NE; NE]<br>0 (0.0)                                                                                | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                             | 0.000 [0.000; NE]<br>0.3163                      |
| Lymphocyte<br>count decreased            | 242/240                      | NE [NE; NE]<br>2 (0.8)                                                                                | 240/237            | NE [NE; NE]<br>3 (1.3)                                                                             | 0.607 [0.101; 3.641]<br>0.5808                   |
| Neutrophil count<br>decreased            | 242/224                      | NE [NE; NE]<br>18 (7.4)                                                                               | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [0.000; NE]<br><.0001                         |
| Platelet count<br>decreased              | 242/225                      | NE [NE; NE]<br>17 (7.0)                                                                               | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [0.000; NE]<br><.0001                         |
| Transaminases<br>increased               | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [0.000; NE]<br>0.4540                         |
| Weight increased                         | 242/242                      | NE [NE; NE]<br>0 (0.0)                                                                                | 240/238            | NE [NE; NE]<br>2 (0.8)                                                                             | 0.000 [0.000; NE]<br>0.1483                      |
| White blood cell<br>count decreased      | 242/237                      | NE [NE; NE]<br>5 (2.1)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [0.000; NE]<br>0.0367                         |
| Metabolism and<br>nutrition<br>disorders | 242/223                      | NE [NE; NE]<br>19 (7.9)                                                                               | 240/228            | NE [NE; NE]<br>12 (5.0)                                                                            | 1.346 [0.650; 2.789]<br>0.4220                   |
| Acidosis                                 | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [0.000; NE]<br>0.3260                         |

| Endpoint<br>SOC<br>PT    | Lurbinectedin + atezolizumab |                                                                                                       | Atezolizumab       |                                                                                                    | Lurbinectedin + atezolizumab vs.<br>atezolizumab |
|--------------------------|------------------------------|-------------------------------------------------------------------------------------------------------|--------------------|----------------------------------------------------------------------------------------------------|--------------------------------------------------|
|                          | N/N <sup>Cen</sup>           | Median time to event in<br>days <sup>a</sup><br>[95% CI] <sup>b</sup><br>patients with event<br>n (%) | N/N <sup>Cen</sup> | Median time to event in days <sup>a</sup><br>[95% CI] <sup>b</sup><br>patients with event<br>n (%) | HR [95% CI] <sup>c</sup><br>p-value <sup>d</sup> |
| Alkalosis                | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [0.000; NE]<br>0.3258                         |
| Decreased<br>appetite    | 242/240                      | NE [NE; NE]<br>2 (0.8)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [0.000; NE]<br>0.1697                         |
| Dehydration              | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [0.000; NE]<br>0.4659                         |
| Diabetes mellitus        | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [0.000; NE]<br>0.3194                         |
| Diabetic<br>ketoacidosis | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [0.000; NE]<br>0.3194                         |
| Hyperglycemia            | 242/239                      | NE [NE; NE]<br>3 (1.2)                                                                                | 240/238            | NE [NE; NE]<br>2 (0.8)                                                                             | 1.307 [0.216; 7.911]<br>0.7704                   |
| Hyperkalemia             | 242/242                      | NE [NE; NE]<br>0 (0.0)                                                                                | 240/238            | NE [NE; NE]<br>2 (0.8)                                                                             | 0.000 [0.000; NE]<br>0.1522                      |
| Hypertriglyceride<br>mia | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [0.000; NE]<br>0.3830                         |
| Hypoalbuminemi<br>a      | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [0.000; NE]<br>0.3237                         |

| Endpoint<br>SOC<br>PT                                 | Lurbinectedin + atezolizumab |                                                                                                       | Atezolizumab       |                                                                                                    | Lurbinectedin + atezolizumab vs.<br>atezolizumab |
|-------------------------------------------------------|------------------------------|-------------------------------------------------------------------------------------------------------|--------------------|----------------------------------------------------------------------------------------------------|--------------------------------------------------|
|                                                       | N/N <sup>Cen</sup>           | Median time to event in<br>days <sup>a</sup><br>[95% CI] <sup>b</sup><br>patients with event<br>n (%) | N/N <sup>Cen</sup> | Median time to event in days <sup>a</sup><br>[95% CI] <sup>b</sup><br>patients with event<br>n (%) | HR [95% CI] <sup>c</sup><br>p-value <sup>d</sup> |
| Hypocalcemia                                          | 242/240                      | NE [NE; NE]<br>2 (0.8)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [0.000; NE]<br>0.2241                         |
| Hypokalemia                                           | 242/236                      | NE [NE; NE]<br>6 (2.5)                                                                                | 240/237            | NE [NE; NE]<br>3 (1.3)                                                                             | 1.644 [0.407; 6.648]<br>0.4809                   |
| Hypomagnesaemia                                       | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [0.000; NE]<br>0.3183                         |
| Hyponatremia                                          | 242/239                      | NE [NE; NE]<br>3 (1.2)                                                                                | 240/235            | NE [NE; NE]<br>5 (2.1)                                                                             | 0.465 [0.109; 1.971]<br>0.2873                   |
| Musculoskeletal<br>and connective<br>tissue disorders | 242/237                      | NE [NE; NE]<br>5 (2.1)                                                                                | 240/236            | NE [NE; NE]<br>4 (1.7)                                                                             | 1.030 [0.273; 3.882]<br>0.9648                   |
| Arthralgia                                            | 242/239                      | NE [NE; NE]<br>3 (1.2)                                                                                | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                             | 2.230 [0.227; 21.901]<br>0.4806                  |
| Back pain                                             | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                             | 0.989 [0.062; 15.817]<br>0.9939                  |
| Mobility<br>decreased                                 | 242/242                      | NE [NE; NE]<br>0 (0.0)                                                                                | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                             | 0.000 [0.000; NE]<br>0.3132                      |
| Osteonecrosis of<br>jaw                               | 242/242                      | NE [NE; NE]<br>0 (0.0)                                                                                | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                             | 0.000 [0.000; NE]<br>0.3142                      |

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| Endpoint<br>SOC<br>PT                                                        | Lurbinectedin + atezolizumab |                                                                                                       | Atezolizumab       |                                                                                                    | Lurbinectedin + atezolizumab vs.<br>atezolizumab |
|------------------------------------------------------------------------------|------------------------------|-------------------------------------------------------------------------------------------------------|--------------------|----------------------------------------------------------------------------------------------------|--------------------------------------------------|
|                                                                              | N/N <sup>Cen</sup>           | Median time to event in<br>days <sup>a</sup><br>[95% CI] <sup>b</sup><br>patients with event<br>n (%) | N/N <sup>Cen</sup> | Median time to event in days <sup>a</sup><br>[95% CI] <sup>b</sup><br>patients with event<br>n (%) | HR [95% CI] <sup>c</sup><br>p-value <sup>d</sup> |
| Pain in extremity                                                            | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [0.000; NE]<br>0.4281                         |
| Neoplasms benign,<br>malignant and<br>unspecified (incl<br>cysts and polyps) | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [0.000; NE]<br>0.4142                         |
| Acute myeloid<br>leukemia                                                    | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [0.000; NE]<br>0.4142                         |
| Nervous system<br>disorders                                                  | 242/235                      | NE [NE; NE]<br>7 (2.9)                                                                                | 240/233            | NE [NE; NE]<br>7 (2.9)                                                                             | 0.715 [0.248; 2.062]<br>0.5333                   |
| Cerebrovascular<br>accident                                                  | 242/242                      | NE [NE; NE]<br>0 (0.0)                                                                                | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                             | 0.000 [0.000; NE]<br>0.3163                      |
| Dizziness                                                                    | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [0.000; NE]<br>0.4687                         |
| Hypoaesthesia                                                                | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [0.000; NE]<br>0.3183                         |
| Nervous system<br>disorder                                                   | 242/242                      | NE [NE; NE]<br>0 (0.0)                                                                                | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                             | 0.000 [0.000; NE]<br>0.1717                      |

| Endpoint<br>SOC<br>PT               | Lurbinectedin + atezolizumab |                                                                                                       | Atezolizumab       |                                                                                                    | Lurbinectedin + atezolizumab vs.<br>atezolizumab |
|-------------------------------------|------------------------------|-------------------------------------------------------------------------------------------------------|--------------------|----------------------------------------------------------------------------------------------------|--------------------------------------------------|
|                                     | N/N <sup>Cen</sup>           | Median time to event in<br>days <sup>a</sup><br>[95% CI] <sup>b</sup><br>patients with event<br>n (%) | N/N <sup>Cen</sup> | Median time to event in days <sup>a</sup><br>[95% CI] <sup>b</sup><br>patients with event<br>n (%) | HR [95% CI] <sup>c</sup><br>p-value <sup>d</sup> |
| Neuralgia                           | 242/242                      | NE [NE; NE]<br>0 (0.0)                                                                                | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                             | 0.000 [0.000; NE]<br>0.2691                      |
| Neuropathy<br>peripheral            | 242/242                      | NE [NE; NE]<br>0 (0.0)                                                                                | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                             | 0.000 [0.000; NE]<br>0.3132                      |
| Peripheral motor<br>neuropathy      | 242/242                      | NE [NE; NE]<br>0 (0.0)                                                                                | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                             | 0.000 [0.000; NE]<br>0.1588                      |
| Peripheral<br>sensory<br>neuropathy | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [0.000; NE]<br>0.3313                         |
| Sciatica                            | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [0.000; NE]<br>0.4435                         |
| Seizure                             | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [0.000; NE]<br>0.4752                         |
| Spinal cord<br>compression          | 242/242                      | NE [NE; NE]<br>0 (0.0)                                                                                | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                             | 0.000 [0.000; NE]<br>0.3086                      |
| Syncope                             | 242/240                      | NE [NE; NE]<br>2 (0.8)                                                                                | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                             | 1.391 [0.124; 15.651]<br>0.7886                  |
| Psychiatric<br>disorders            | 242/240                      | NE [NE; NE]<br>2 (0.8)                                                                                | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                             | 1.043 [0.095; 11.503]<br>0.9725                  |

| Endpoint<br>SOC<br>PT       | Lurbinectedin + atezolizumab |                                                                                                       | Atezolizumab       |                                                                                                    | Lurbinectedin + atezolizumab vs.<br>atezolizumab |
|-----------------------------|------------------------------|-------------------------------------------------------------------------------------------------------|--------------------|----------------------------------------------------------------------------------------------------|--------------------------------------------------|
|                             | N/N <sup>Cen</sup>           | Median time to event in<br>days <sup>a</sup><br>[95% CI] <sup>b</sup><br>patients with event<br>n (%) | N/N <sup>Cen</sup> | Median time to event in days <sup>a</sup><br>[95% CI] <sup>b</sup><br>patients with event<br>n (%) | HR [95% CI] <sup>c</sup><br>p-value <sup>d</sup> |
| Completed suicide           | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [0.000; NE]<br>0.4751                         |
| Delirium                    | 242/242                      | NE [NE; NE]<br>0 (0.0)                                                                                | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                             | 0.000 [0.000; NE]<br>0.1621                      |
| Depression                  | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [0.000; NE]<br>0.4553                         |
| Renal and urinary disorders | 242/235                      | NE [NE; NE]<br>7 (2.9)                                                                                | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                             | 5.997 [0.733; 49.038]<br>0.0577                  |
| Acute kidney injury         | 242/239                      | NE [NE; NE]<br>3 (1.2)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [0.000; NE]<br>0.0969                         |
| Immune-mediated nephritis   | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [0.000; NE]<br>0.4435                         |
| Nephropathy                 | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [0.000; NE]<br>0.3183                         |
| Perinephric collection      | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [0.000; NE]<br>0.4734                         |
| Renal failure               | 242/240                      | NE [NE; NE]<br>2 (0.8)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [0.000; NE]<br>0.2210                         |

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| Endpoint<br>SOC<br>PT                                    | Lurbinectedin + atezolizumab |                                                                                                       | Atezolizumab       |                                                                                                    | Lurbinectedin + atezolizumab vs.<br>atezolizumab |
|----------------------------------------------------------|------------------------------|-------------------------------------------------------------------------------------------------------|--------------------|----------------------------------------------------------------------------------------------------|--------------------------------------------------|
|                                                          | N/N <sup>Cen</sup>           | Median time to event in<br>days <sup>a</sup><br>[95% CI] <sup>b</sup><br>patients with event<br>n (%) | N/N <sup>Cen</sup> | Median time to event in days <sup>a</sup><br>[95% CI] <sup>b</sup><br>patients with event<br>n (%) | HR [95% CI] <sup>c</sup><br>p-value <sup>d</sup> |
| Urinary retention                                        | 242/242                      | NE [NE; NE]<br>0 (0.0)                                                                                | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                             | 0.000 [0.000; NE]<br>0.3163                      |
| Respiratory,<br>thoracic and<br>mediastinal<br>disorders | 242/227                      | NE [NE; NE]<br>15 (6.2)                                                                               | 240/234            | NE [NE; NE]<br>6 (2.5)                                                                             | 2.112 [0.815; 5.475]<br>0.1158                   |
| Asthma                                                   | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [0.000; NE]<br>0.3193                         |
| Bronchospasm                                             | 242/242                      | NE [NE; NE]<br>0 (0.0)                                                                                | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                             | 0.000 [0.000; NE]<br>0.3163                      |
| Dyspnea                                                  | 242/236                      | NE [NE; NE]<br>6 (2.5)                                                                                | 240/236            | NE [NE; NE]<br>4 (1.7)                                                                             | 1.209 [0.337; 4.333]<br>0.7704                   |
| Hemoptysis                                               | 242/240                      | NE [NE; NE]<br>2 (0.8)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [0.000; NE]<br>0.2054                         |
| Hypoxia                                                  | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                             | 0.718 [0.044; 11.839]<br>0.8163                  |
| Immune-<br>mediated lung<br>disease                      | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [0.000; NE]<br>0.3193                         |

| Endpoint<br>SOC<br>PT                  | Lurbinectedin + atezolizumab |                                                                                                       | Atezolizumab       |                                                                                                    | Lurbinectedin + atezolizumab vs.<br>atezolizumab |
|----------------------------------------|------------------------------|-------------------------------------------------------------------------------------------------------|--------------------|----------------------------------------------------------------------------------------------------|--------------------------------------------------|
|                                        | N/N <sup>Cen</sup>           | Median time to event in<br>days <sup>a</sup><br>[95% CI] <sup>b</sup><br>patients with event<br>n (%) | N/N <sup>Cen</sup> | Median time to event in days <sup>a</sup><br>[95% CI] <sup>b</sup><br>patients with event<br>n (%) | HR [95% CI] <sup>c</sup><br>p-value <sup>d</sup> |
| Pleural effusion                       | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [0.000; NE]<br>0.3579                         |
| Pneumonitis                            | 242/240                      | NE [NE; NE]<br>2 (0.8)                                                                                | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                             | 1.634 [0.145; 18.402]<br>0.6882                  |
| Productive cough                       | 242/242                      | NE [NE; NE]<br>0 (0.0)                                                                                | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                             | 0.000 [0.000; NE]<br>0.1573                      |
| Pulmonary embolism                     | 242/239                      | NE [NE; NE]<br>3 (1.2)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [0.000; NE]<br>0.1245                         |
| Respiratory failure                    | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [0.000; NE]<br>0.3237                         |
| Skin and subcutaneous tissue disorders | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                             | 0.549 [0.034; 8.791]<br>0.6669                   |
| Pruritus                               | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [0.000; NE]<br>0.4334                         |
| Superficial inflammatory dermatosis    | 242/242                      | NE [NE; NE]<br>0 (0.0)                                                                                | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                             | 0.000 [0.000; NE]<br>0.1613                      |
| Vascular disorders                     | 242/237                      | NE [NE; NE]<br>5 (2.1)                                                                                | 240/237            | NE [NE; NE]<br>3 (1.3)                                                                             | 1.224 [0.288; 5.199]<br>0.7834                   |

| Endpoint<br>SOC<br>PT                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | Lurbinectedin + atezolizumab |                                                                                                       | Atezolizumab       |                                                                                                    | Lurbinectedin + atezolizumab vs.<br>atezolizumab |
|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------|-------------------------------------------------------------------------------------------------------|--------------------|----------------------------------------------------------------------------------------------------|--------------------------------------------------|
|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | N/N <sup>Cen</sup>           | Median time to event in<br>days <sup>a</sup><br>[95% CI] <sup>b</sup><br>patients with event<br>n (%) | N/N <sup>Cen</sup> | Median time to event in days <sup>a</sup><br>[95% CI] <sup>b</sup><br>patients with event<br>n (%) | HR [95% CI] <sup>c</sup><br>p-value <sup>d</sup> |
| Arteriosclerosis                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [0.000; NE]<br>0.4435                         |
| Hypertension                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         | 242/242                      | NE [NE; NE]<br>0 (0.0)                                                                                | 240/237            | NE [NE; NE]<br>3 (1.3)                                                                             | 0.000 [0.000; NE]<br>0.0474                      |
| Hypotension                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [0.000; NE]<br>0.4386                         |
| Hypovolemic<br>shock                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [0.000; NE]<br>0.4659                         |
| Thrombophlebitis                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [0.000; NE]<br>0.3313                         |
| Thrombosis                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [0.000; NE]<br>0.3194                         |
| <p>CCOD: 12 February 2025; NE: not estimable.</p> <p>If a patient experienced either repeated occurrences of the same adverse event or two different adverse events, one Grade 3 and one Grade 4, they are counted only once in the Grade <math>\geq 3</math> category.</p> <p>a: summaries of duration (median) are Kaplan-Meier estimates.</p> <p>b: 95% CIs for the median were computed using the method of Brookmeyer and Crowley.</p> <p>c: hazard ratios were estimated using a stratified Cox proportional hazard model. The stratification factors are ECOG PS at randomization (0 vs. 1), LDH at randomization (<math>\leq</math>ULN vs <math>&gt;</math>ULN) via local laboratory test, presence of liver metastases at enrollment (yes vs. no), and prior receipt of PCI (yes vs. no).</p> <p>d: p-value based on the log rank test.</p> |                              |                                                                                                       |                    |                                                                                                    |                                                  |

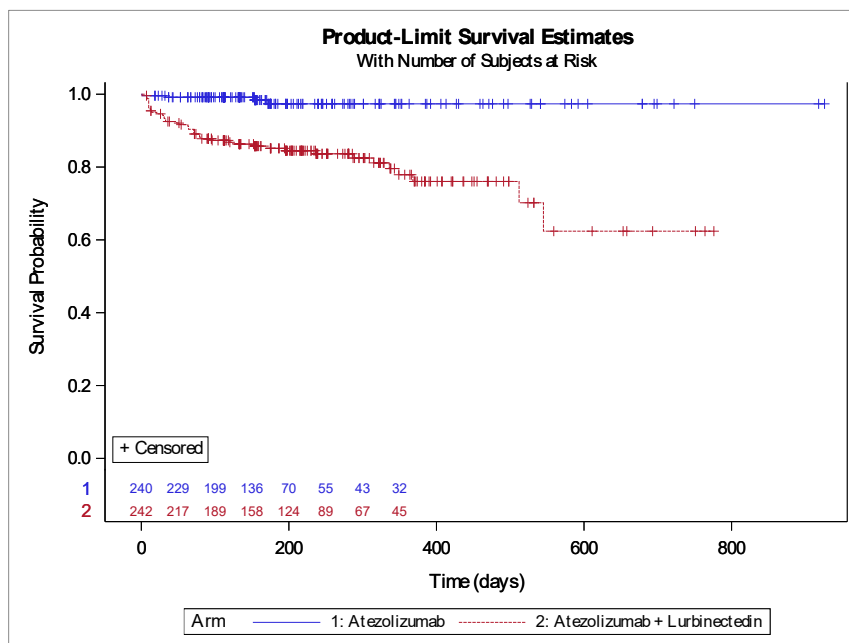


Abbildung 132: Kaplan-Meier plot for grade  $\geq 3$  AE (SOC blood and lymphatic system disorders), IMforte trial, Safety Analysis Set, CCOD 12 February 2025

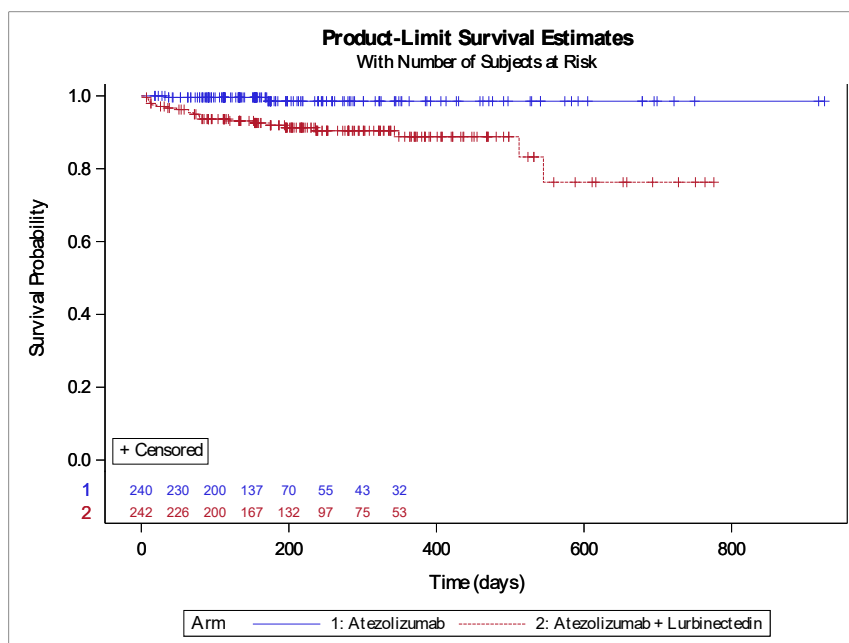


Abbildung 133: Kaplan-Meier plot for grade  $\geq 3$  AE (PT anemia), IMforte trial, Safety Analysis Set, CCOD 12 February 2025

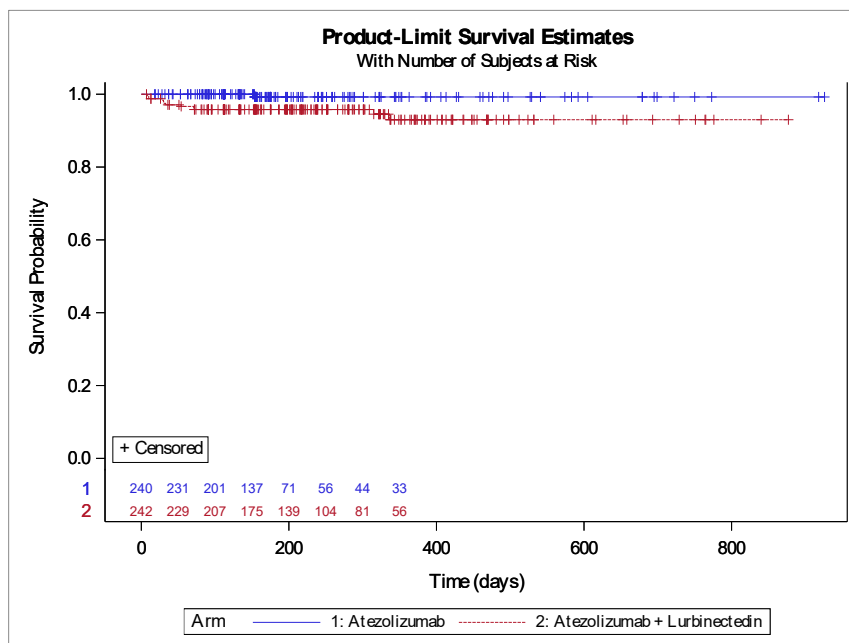


Abbildung 134: Kaplan-Meier plot for grade  $\geq 3$  AE (PT neutropenia), IMforte trial, Safety Analysis Set, CCOD 12 February 2025

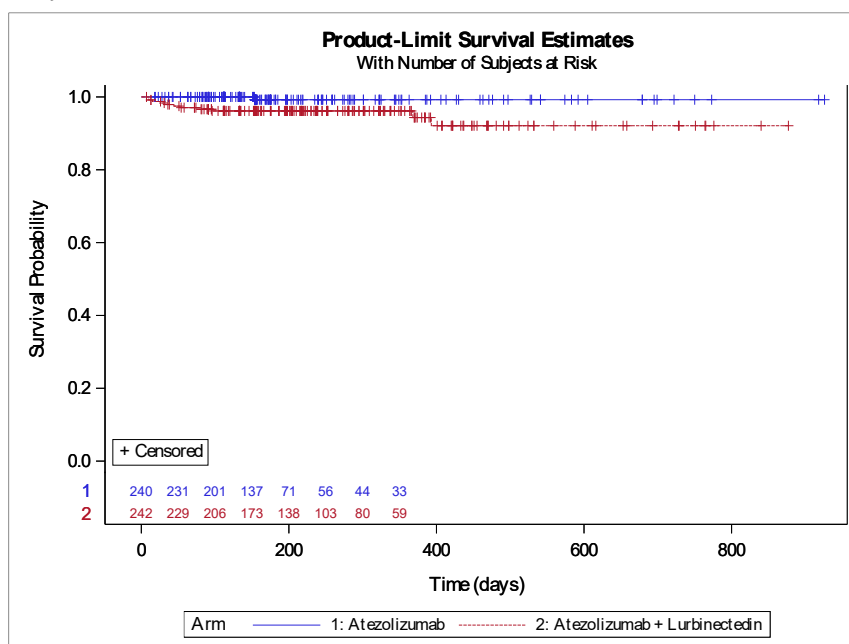


Abbildung 135: Kaplan-Meier plot for grade  $\geq 3$  AE (PT thrombocytopenia), IMforte trial, Safety Analysis Set, CCOD 12 February 2025

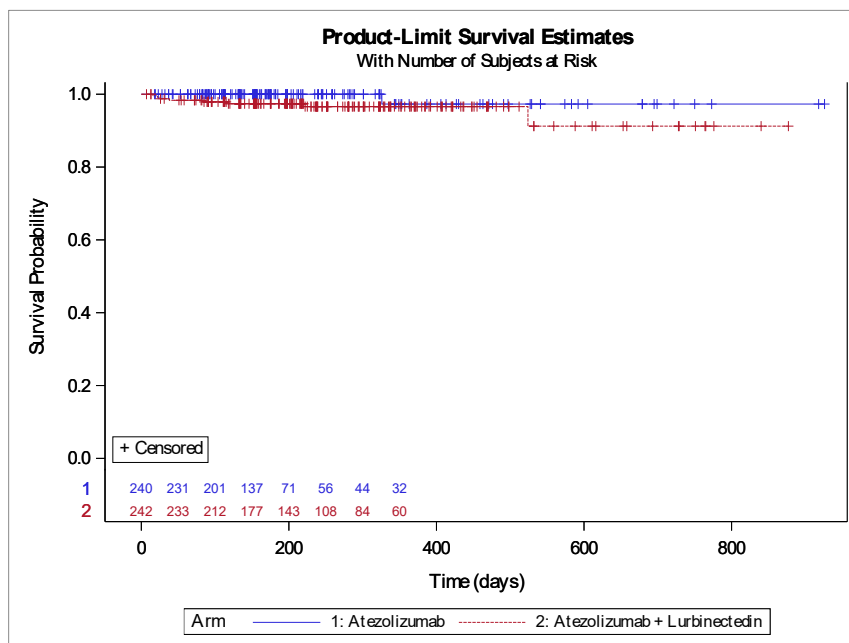


Abbildung 136: Kaplan-Meier plot for grade  $\geq 3$  AE (SOC cardiac disorders), IMforte trial, Safety Analysis Set, CCOD 12 February 2025

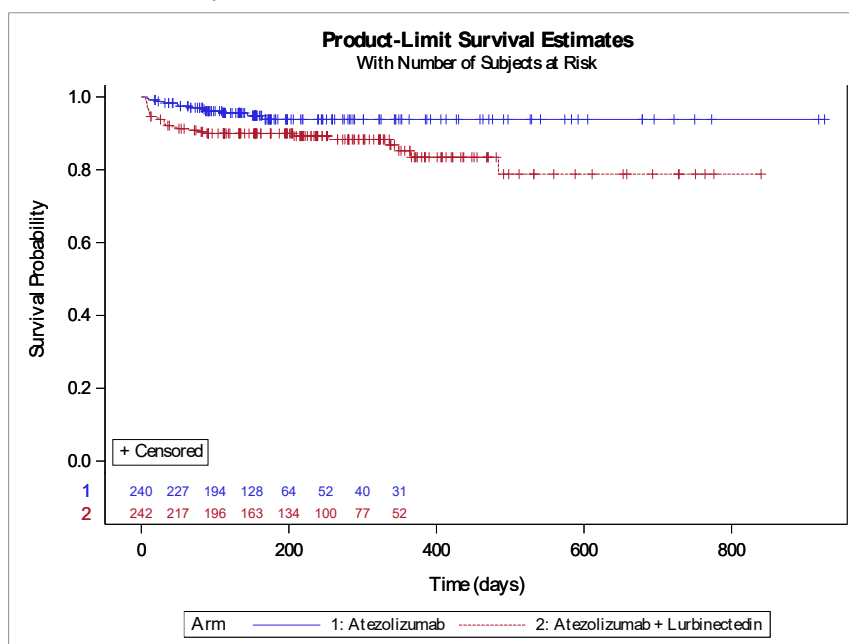


Abbildung 137: Kaplan-Meier plot for grade  $\geq 3$  AE (SOC investigations), IMforte trial, Safety Analysis Set, CCOD 12 February 2025

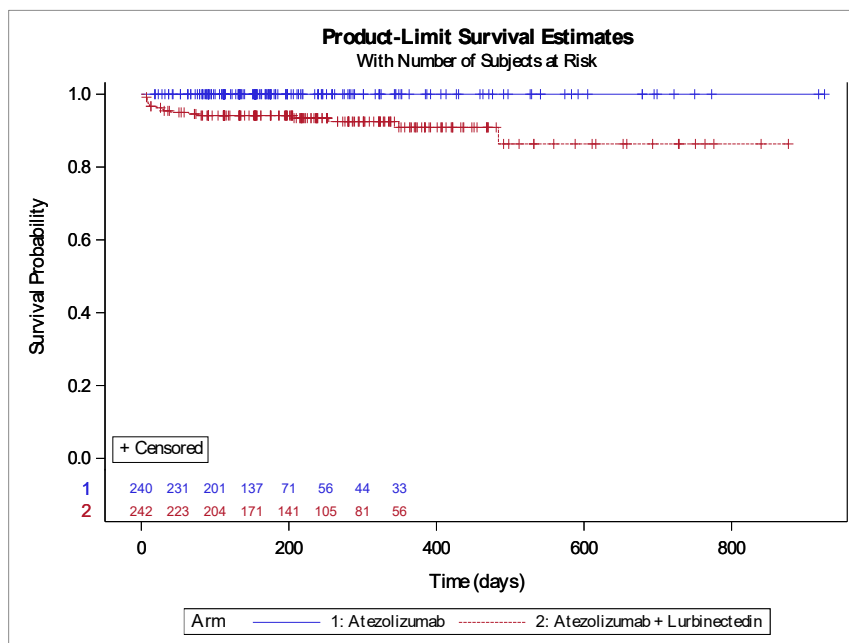


Abbildung 138: Kaplan-Meier plot for grade  $\geq 3$  AE (PT neutrophil count decreased), IMforte trial, Safety Analysis Set, CCOD 12 February 2025

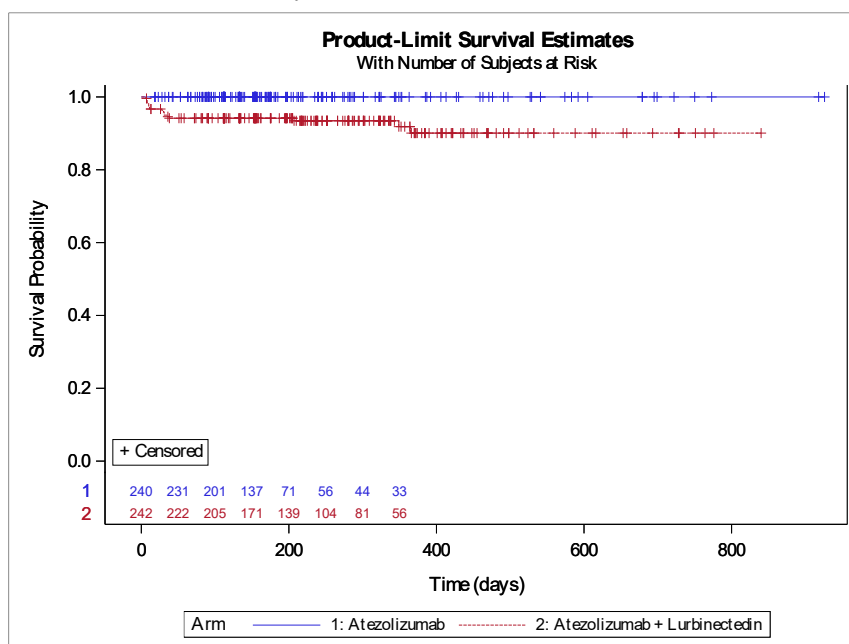


Abbildung 139: Kaplan-Meier plot for grade  $\geq 3$  AE (PT platelet count decreased), IMforte trial, Safety Analysis Set, CCOD 12 February 2025

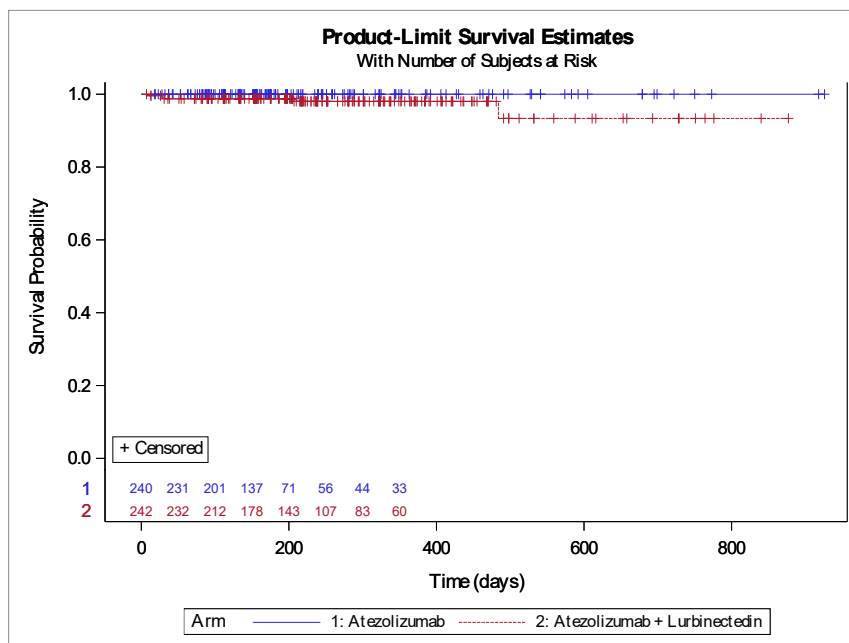


Abbildung 140: Kaplan-Meier plot for grade  $\geq 3$  AE (PT white blood cell count decreased), IMforte trial, Safety Analysis Set, CCOD 12 February 2025

Tabelle 12: Grade 5 severe AE (death related to AE) by SOC and PT including effect estimates

| Endpoint<br>SOC<br>PT                                         | Lurbinectedin + atezolizumab |                                                                                                       | Atezolizumab       |                                                                                                    | Lurbinectedin + atezolizumab vs.<br>atezolizumab |
|---------------------------------------------------------------|------------------------------|-------------------------------------------------------------------------------------------------------|--------------------|----------------------------------------------------------------------------------------------------|--------------------------------------------------|
|                                                               | N/N <sup>Cen</sup>           | Median time to event in<br>days <sup>a</sup><br>[95% CI] <sup>b</sup><br>patients with event<br>n (%) | N/N <sup>Cen</sup> | Median time to event in days <sup>a</sup><br>[95% CI] <sup>b</sup><br>patients with event<br>n (%) | HR [95% CI] <sup>c</sup><br>p-value <sup>d</sup> |
| Blood and<br>lymphatic<br>system disorders                    | 242/240                      | NE [NE; NE]<br>2 (0.8)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [0.000; NE]<br>0.1595                         |
| Febrile<br>neutropenia                                        | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [0.000; NE]<br>0.3205                         |
| Neutropenia                                                   | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [0.000; NE]<br>0.3194                         |
| Cardiac<br>disorders                                          | 242/238                      | NE [NE; NE]<br>4 (1.7)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [0.000; NE]<br>0.0663                         |
| Cardio-<br>respiratory<br>arrest                              | 242/240                      | NE [NE; NE]<br>2 (0.8)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [0.000; NE]<br>0.1624                         |
| Myocardial<br>infarction                                      | 242/240                      | NE [NE; NE]<br>2 (0.8)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [0.000; NE]<br>0.2311                         |
| General<br>disorders and<br>administration<br>site conditions | 242/242                      | NE [NE; NE]<br>0 (0.0)                                                                                | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                             | 0.000 [0.000; NE]<br>0.1886                      |
| Death                                                         | 242/242                      | NE [NE; NE]<br>0 (0.0)                                                                                | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                             | 0.000 [0.000; NE]<br>0.1886                      |

| Endpoint<br>SOC<br>PT           | Lurbinectedin + atezolizumab |                                                                                                       | Atezolizumab       |                                                                                                    | Lurbinectedin + atezolizumab vs.<br>atezolizumab |
|---------------------------------|------------------------------|-------------------------------------------------------------------------------------------------------|--------------------|----------------------------------------------------------------------------------------------------|--------------------------------------------------|
|                                 | N/N <sup>Cen</sup>           | Median time to event in<br>days <sup>a</sup><br>[95% CI] <sup>b</sup><br>patients with event<br>n (%) | N/N <sup>Cen</sup> | Median time to event in days <sup>a</sup><br>[95% CI] <sup>b</sup><br>patients with event<br>n (%) | HR [95% CI] <sup>c</sup><br>p-value <sup>d</sup> |
| Infections and<br>infestations  | 242/237                      | NE [NE; NE]<br>5 (2.1)                                                                                | 240/236            | NE [NE; NE]<br>4 (1.7)                                                                             | 1.071 [0.284; 4.037]<br>0.9186                   |
| Abscess<br>intestinal           | 242/242                      | NE [NE; NE]<br>0 (0.0)                                                                                | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                             | 0.000 [0.000; NE]<br>0.3183                      |
| COVID-19<br>pneumonia           | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [0.000; NE]<br>0.3193                         |
| Pneumonia                       | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/238            | NE [NE; NE]<br>2 (0.8)                                                                             | 0.387 [0.034; 4.391]<br>0.4276                   |
| Pneumonia<br>viral              | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [0.000; NE]<br>0.3193                         |
| Sepsis                          | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                             | 0.711 [0.043; 11.771]<br>0.8112                  |
| Vascular<br>device<br>infection | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [0.000; NE]<br>0.3205                         |
| Nervous system<br>disorders     | 242/242                      | NE [NE; NE]<br>0 (0.0)                                                                                | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                             | 0.000 [0.000; NE]<br>0.3163                      |
| Cerebrovascu-<br>lar accident   | 242/242                      | NE [NE; NE]<br>0 (0.0)                                                                                | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                             | 0.000 [0.000; NE]<br>0.3163                      |

| Endpoint<br>SOC<br>PT                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         | Lurbinectedin + atezolizumab |                                                                                                       | Atezolizumab       |                                                                                                    | Lurbinectedin + atezolizumab vs.<br>atezolizumab |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------|-------------------------------------------------------------------------------------------------------|--------------------|----------------------------------------------------------------------------------------------------|--------------------------------------------------|
|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               | N/N <sup>Cen</sup>           | Median time to event in<br>days <sup>a</sup><br>[95% CI] <sup>b</sup><br>patients with event<br>n (%) | N/N <sup>Cen</sup> | Median time to event in days <sup>a</sup><br>[95% CI] <sup>b</sup><br>patients with event<br>n (%) | HR [95% CI] <sup>c</sup><br>p-value <sup>d</sup> |
| Psychiatric disorders                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [0.000; NE]<br>0.4751                         |
| Completed suicide                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [0.000; NE]<br>0.4751                         |
| CCOD: 12 February 2025; NE: not estimable.<br>a: summaries of duration (median) are Kaplan-Meier estimates.<br>b: 95% CIs for the median were computed using the method of Brookmeyer and Crowley.<br>c: hazard ratios were estimated using a stratified Cox proportional hazard model. The stratification factors are ECOG PS at randomization (0 vs. 1), LDH at randomization ( $\leq$ ULN vs $>$ ULN) via local laboratory test, presence of liver metastases at enrollment (yes vs. no), and prior receipt of PCI (yes vs. no).<br>d: p-value based on the log rank test. |                              |                                                                                                       |                    |                                                                                                    |                                                  |

Tabelle 13: Serious AE by SOC and PT including effect estimates

| Endpoint<br>SOC<br>PT                | Lurbinectedin + atezolizumab |                                                                                                       | Atezolizumab       |                                                                                                       | Lurbinectedin + atezolizumab vs.<br>atezolizumab |
|--------------------------------------|------------------------------|-------------------------------------------------------------------------------------------------------|--------------------|-------------------------------------------------------------------------------------------------------|--------------------------------------------------|
|                                      | N/N <sup>Cen</sup>           | Median time to event in<br>days <sup>a</sup><br>[95% CI] <sup>b</sup><br>patients with event<br>n (%) | N/N <sup>Cen</sup> | Median time to event in<br>days <sup>a</sup><br>[95% CI] <sup>b</sup><br>patients with event<br>n (%) | HR [95% CI] <sup>c</sup><br>p-value <sup>d</sup> |
| Blood and lymphatic system disorders | 242/233                      | NE [NE; NE]<br>9 (3.7)                                                                                | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                                | 7.868 [0.993; 62.318]<br>0.0207                  |
| Anemia                               | 242/240                      | NE [NE; NE]<br>2 (0.8)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                                | NE [0.000; NE]<br>0.2414                         |
| Febrile neutropenia                  | 242/238                      | NE [NE; NE]<br>4 (1.7)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                                | NE [0.000; NE]<br>0.0504                         |
| Lymphadenitis                        | 242/242                      | NE [NE; NE]<br>0 (0.0)                                                                                | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                                | 0.000 [0.000; NE]<br>0.3153                      |
| Neutropenia                          | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                                | NE [0.000; NE]<br>0.3194                         |
| Pancytopenia                         | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                                | NE [0.000; NE]<br>0.4540                         |
| Thrombocytopenia                     | 242/240                      | NE [NE; NE]<br>2 (0.8)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                                | NE [0.000; NE]<br>0.1600                         |
| Cardiac disorders                    | 242/234                      | NE [NE; NE]<br>8 (3.3)                                                                                | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                                | 6.758 [0.841; 54.317]<br>0.0378                  |
| Acute myocardial infarction          | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                                | NE [0.000; NE]<br>0.3574                         |

| Endpoint<br>SOC<br>PT         | Lurbinectedin + atezolizumab |                                                                                                       | Atezolizumab       |                                                                                                       | Lurbinectedin + atezolizumab vs.<br>atezolizumab |
|-------------------------------|------------------------------|-------------------------------------------------------------------------------------------------------|--------------------|-------------------------------------------------------------------------------------------------------|--------------------------------------------------|
|                               | N/N <sup>Cen</sup>           | Median time to event in<br>days <sup>a</sup><br>[95% CI] <sup>b</sup><br>patients with event<br>n (%) | N/N <sup>Cen</sup> | Median time to event in<br>days <sup>a</sup><br>[95% CI] <sup>b</sup><br>patients with event<br>n (%) | HR [95% CI] <sup>c</sup><br>p-value <sup>d</sup> |
| Atrial fibrillation           | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                                | NE [0.000; NE]<br>0.3163                         |
| Cardio-<br>respiratory arrest | 242/240                      | NE [NE; NE]<br>2 (0.8)                                                                                | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                                | 1.608 [0.143; 18.122]<br>0.6980                  |
| Myocardial<br>infarction      | 242/239                      | NE [NE; NE]<br>3 (1.2)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                                | NE [0.000; NE]<br>0.1201                         |
| Palpitations                  | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                                | NE [0.000; NE]<br>0.3586                         |
| Endocrine disorders           | 242/242                      | NE [NE; NE]<br>0 (0.0)                                                                                | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                                | 0.000 [0.000; NE]<br>0.3131                      |
| Adrenal<br>insufficiency      | 242/242                      | NE [NE; NE]<br>0 (0.0)                                                                                | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                                | 0.000 [0.000; NE]<br>0.3131                      |
| Gastrointestinal<br>disorders | 242/233                      | NE [NE; NE]<br>9 (3.7)                                                                                | 240/230            | NE [NE; NE]<br>10 (4.2)                                                                               | 0.788 [0.318; 1.951]<br>0.6059                   |
| Abdominal pain                | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                                | NE [0.000; NE]<br>0.4348                         |
| Abdominal pain<br>upper       | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                                | NE [0.000; NE]<br>0.3183                         |

| Endpoint<br>SOC<br>PT                   | Lurbinectedin + atezolizumab |                                                                                                       | Atezolizumab       |                                                                                                       | Lurbinectedin + atezolizumab vs.<br>atezolizumab |
|-----------------------------------------|------------------------------|-------------------------------------------------------------------------------------------------------|--------------------|-------------------------------------------------------------------------------------------------------|--------------------------------------------------|
|                                         | N/N <sup>Cen</sup>           | Median time to event in<br>days <sup>a</sup><br>[95% CI] <sup>b</sup><br>patients with event<br>n (%) | N/N <sup>Cen</sup> | Median time to event in<br>days <sup>a</sup><br>[95% CI] <sup>b</sup><br>patients with event<br>n (%) | HR [95% CI] <sup>c</sup><br>p-value <sup>d</sup> |
| Chronic gastritis                       | 242/242                      | NE [NE; NE]<br>0 (0.0)                                                                                | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                                | 0.000 [0.000; NE]<br>0.2123                      |
| Colitis                                 | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/238            | NE [NE; NE]<br>2 (0.8)                                                                                | 0.470 [0.043; 5.191]<br>0.5281                   |
| Constipation                            | 242/240                      | NE [NE; NE]<br>2 (0.8)                                                                                | 240/238            | NE [NE; NE]<br>2 (0.8)                                                                                | 0.986 [0.139; 6.998]<br>0.9885                   |
| Diarrhea                                | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                                | NE [0.000; NE]<br>0.4817                         |
| Gastrointestinal<br>hemorrhage          | 242/242                      | NE [NE; NE]<br>0 (0.0)                                                                                | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                                | 0.000 [0.000; NE]<br>0.3110                      |
| Gastrointestinal<br>polyp<br>hemorrhage | 242/242                      | NE [NE; NE]<br>0 (0.0)                                                                                | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                                | 0.000 [0.000; NE]<br>0.1738                      |
| Ileus                                   | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                                | NE [0.000; NE]<br>0.3193                         |
| Intestinal<br>obstruction               | 242/242                      | NE [NE; NE]<br>0 (0.0)                                                                                | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                                | 0.000 [0.000; NE]<br>0.3153                      |
| Nausea                                  | 242/240                      | NE [NE; NE]<br>2 (0.8)                                                                                | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                                | 1.980 [0.180; 21.836]<br>0.5695                  |

| Endpoint<br>SOC<br>PT                                      | Lurbinectedin + atezolizumab |                                                                                                       | Atezolizumab       |                                                                                                       | Lurbinectedin + atezolizumab vs.<br>atezolizumab |
|------------------------------------------------------------|------------------------------|-------------------------------------------------------------------------------------------------------|--------------------|-------------------------------------------------------------------------------------------------------|--------------------------------------------------|
|                                                            | N/N <sup>Cen</sup>           | Median time to event in<br>days <sup>a</sup><br>[95% CI] <sup>b</sup><br>patients with event<br>n (%) | N/N <sup>Cen</sup> | Median time to event in<br>days <sup>a</sup><br>[95% CI] <sup>b</sup><br>patients with event<br>n (%) | HR [95% CI] <sup>c</sup><br>p-value <sup>d</sup> |
| Pancreatitis acute                                         | 242/242                      | NE [NE; NE]<br>0 (0.0)                                                                                | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                                | 0.000 [0.000; NE]<br>0.3152                      |
| Volvulus                                                   | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                                | 0.735 [0.045; 12.100]<br>0.8288                  |
| General disorders<br>and administration<br>site conditions | 242/235                      | NE [NE; NE]<br>7 (2.9)                                                                                | 240/237            | NE [NE; NE]<br>3 (1.3)                                                                                | 1.848 [0.472; 7.241]<br>0.3707                   |
| Adhesion                                                   | 242/242                      | NE [NE; NE]<br>0 (0.0)                                                                                | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                                | 0.000 [0.000; NE]<br>0.1613                      |
| Administration<br>site extravasation                       | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                                | NE [0.000; NE]<br>0.3183                         |
| Chest pain                                                 | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                                | 0.706 [0.043; 11.742]<br>0.8077                  |
| Death                                                      | 242/242                      | NE [NE; NE]<br>0 (0.0)                                                                                | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                                | 0.000 [0.000; NE]<br>0.1886                      |
| Fatigue                                                    | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                                | NE [0.000; NE]<br>0.3194                         |
| Oedema<br>peripheral                                       | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                                | NE [0.000; NE]<br>0.4752                         |

| Endpoint<br>SOC<br>PT            | Lurbinectedin + atezolizumab |                                                                                                       | Atezolizumab       |                                                                                                       | Lurbinectedin + atezolizumab vs.<br>atezolizumab |
|----------------------------------|------------------------------|-------------------------------------------------------------------------------------------------------|--------------------|-------------------------------------------------------------------------------------------------------|--------------------------------------------------|
|                                  | N/N <sup>Cen</sup>           | Median time to event in<br>days <sup>a</sup><br>[95% CI] <sup>b</sup><br>patients with event<br>n (%) | N/N <sup>Cen</sup> | Median time to event in<br>days <sup>a</sup><br>[95% CI] <sup>b</sup><br>patients with event<br>n (%) | HR [95% CI] <sup>c</sup><br>p-value <sup>d</sup> |
| Pain                             | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                                | NE [0.000; NE]<br>0.3205                         |
| Pyrexia                          | 242/240                      | NE [NE; NE]<br>2 (0.8)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                                | NE [0.000; NE]<br>0.1582                         |
| Hepatobiliary<br>disorders       | 242/240                      | NE [NE; NE]<br>2 (0.8)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                                | NE [0.000; NE]<br>0.1623                         |
| Cholecystitis                    | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                                | NE [0.000; NE]<br>0.3237                         |
| Immune-<br>mediated<br>hepatitis | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                                | NE [0.000; NE]<br>0.3237                         |
| Infections and<br>infestations   | 242/213                      | NE [NE; NE]<br>29 (12.0)                                                                              | 240/224            | NE [NE; NE]<br>16 (6.7)                                                                               | 1.543 [0.835; 2.852]<br>0.1634                   |
| Abscess intestinal               | 242/242                      | NE [NE; NE]<br>0 (0.0)                                                                                | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                                | 0.000 [0.000; NE]<br>0.3183                      |
| Atypical<br>pneumonia            | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                                | NE [0.000; NE]<br>0.3193                         |
| Bacteroides<br>infection         | 242/242                      | NE [NE; NE]<br>0 (0.0)                                                                                | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                                | 0.000 [0.000; NE]<br>0.3183                      |

| Endpoint<br>SOC<br>PT                | Lurbinectedin + atezolizumab |                                                                                                       | Atezolizumab       |                                                                                                       | Lurbinectedin + atezolizumab vs.<br>atezolizumab |
|--------------------------------------|------------------------------|-------------------------------------------------------------------------------------------------------|--------------------|-------------------------------------------------------------------------------------------------------|--------------------------------------------------|
|                                      | N/N <sup>Cen</sup>           | Median time to event in<br>days <sup>a</sup><br>[95% CI] <sup>b</sup><br>patients with event<br>n (%) | N/N <sup>Cen</sup> | Median time to event in<br>days <sup>a</sup><br>[95% CI] <sup>b</sup><br>patients with event<br>n (%) | HR [95% CI] <sup>c</sup><br>p-value <sup>d</sup> |
| Bronchitis                           | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                                | NE [0.000; NE]<br>0.4684                         |
| Bursitis infective                   | 242/242                      | NE [NE; NE]<br>0 (0.0)                                                                                | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                                | 0.000 [0.000; NE]<br>0.1981                      |
| COVID-19                             | 242/240                      | NE [NE; NE]<br>2 (0.8)                                                                                | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                                | 1.969 [0.179; 21.709]<br>0.5729                  |
| COVID-19<br>pneumonia                | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                                | NE [0.000; NE]<br>0.3193                         |
| Cellulitis                           | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                                | NE [0.000; NE]<br>0.3204                         |
| Encephalitis                         | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                                | 0.860 [0.054; 13.744]<br>0.9148                  |
| Febrile infection                    | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                                | NE [0.000; NE]<br>0.3258                         |
| Infection                            | 242/239                      | NE [NE; NE]<br>3 (1.2)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                                | NE [0.000; NE]<br>0.0839                         |
| Lower respiratory<br>tract infection | 242/240                      | NE [NE; NE]<br>2 (0.8)                                                                                | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                                | 1.963 [0.178; 21.643]<br>0.5747                  |

| Endpoint<br>SOC<br>PT                                | Lurbinectedin + atezolizumab |                                                                                                       | Atezolizumab       |                                                                                                       | Lurbinectedin + atezolizumab vs.<br>atezolizumab |
|------------------------------------------------------|------------------------------|-------------------------------------------------------------------------------------------------------|--------------------|-------------------------------------------------------------------------------------------------------|--------------------------------------------------|
|                                                      | N/N <sup>Cen</sup>           | Median time to event in<br>days <sup>a</sup><br>[95% CI] <sup>b</sup><br>patients with event<br>n (%) | N/N <sup>Cen</sup> | Median time to event in<br>days <sup>a</sup><br>[95% CI] <sup>b</sup><br>patients with event<br>n (%) | HR [95% CI] <sup>c</sup><br>p-value <sup>d</sup> |
| Pharyngitis                                          | 242/242                      | NE [NE; NE]<br>0 (0.0)                                                                                | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                                | 0.000 [0.000; NE]<br>0.2768                      |
| Pneumocystis<br>jirovecii<br>pneumonia               | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                                | NE [0.000; NE]<br>0.3183                         |
| Pneumonia                                            | 242/235                      | NE [NE; NE]<br>7 (2.9)                                                                                | 240/234            | NE [NE; NE]<br>6 (2.5)                                                                                | 0.964 [0.321; 2.898]<br>0.9487                   |
| Pneumonia viral                                      | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                                | NE [0.000; NE]<br>0.3193                         |
| Respiratory tract<br>infection                       | 242/237                      | NE [NE; NE]<br>5 (2.1)                                                                                | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                                | 3.562 [0.413; 30.724]<br>0.2175                  |
| Sepsis                                               | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                                | 0.711 [0.043; 11.771]<br>0.8112                  |
| Urinary tract<br>infection                           | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                                | 0.863 [0.054; 13.872]<br>0.9168                  |
| Vascular device<br>infection                         | 242/239                      | NE [NE; NE]<br>3 (1.2)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                                | NE [0.000; NE]<br>0.1545                         |
| Injury, poisoning<br>and procedural<br>complications | 242/240                      | NE [NE; NE]<br>2 (0.8)                                                                                | 240/238            | NE [NE; NE]<br>2 (0.8)                                                                                | 0.753 [0.104; 5.445]<br>0.7777                   |

| Endpoint<br>SOC<br>PT                        | Lurbinectedin + atezolizumab |                                                                                                       | Atezolizumab       |                                                                                                       | Lurbinectedin + atezolizumab vs.<br>atezolizumab |
|----------------------------------------------|------------------------------|-------------------------------------------------------------------------------------------------------|--------------------|-------------------------------------------------------------------------------------------------------|--------------------------------------------------|
|                                              | N/N <sup>Cen</sup>           | Median time to event in<br>days <sup>a</sup><br>[95% CI] <sup>b</sup><br>patients with event<br>n (%) | N/N <sup>Cen</sup> | Median time to event in<br>days <sup>a</sup><br>[95% CI] <sup>b</sup><br>patients with event<br>n (%) | HR [95% CI] <sup>c</sup><br>p-value <sup>d</sup> |
| Ankle fracture                               | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                                | NE [0.000; NE]<br>0.4781                         |
| Femur fracture                               | 242/242                      | NE [NE; NE]<br>0 (0.0)                                                                                | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                                | 0.000 [0.000; NE]<br>0.3153                      |
| Hip fracture                                 | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                                | NE [0.000; NE]<br>0.3966                         |
| Road traffic<br>accident                     | 242/242                      | NE [NE; NE]<br>0 (0.0)                                                                                | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                                | 0.000 [0.000; NE]<br>0.3047                      |
| Investigations                               | 242/236                      | NE [NE; NE]<br>6 (2.5)                                                                                | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                                | 5.446 [0.653; 45.418]<br>0.0788                  |
| Alanine<br>aminotransferase<br>increased     | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                                | NE [0.000; NE]<br>0.3194                         |
| Aspartate<br>aminotransferase<br>increased   | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                                | NE [0.000; NE]<br>0.3194                         |
| Blood bilirubin<br>increased                 | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                                | NE [0.000; NE]<br>0.3258                         |
| Blood creatine<br>phosphokinase<br>increased | 242/242                      | NE [NE; NE]<br>0 (0.0)                                                                                | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                                | 0.000 [0.000; NE]<br>0.3110                      |

| Endpoint<br>SOC<br>PT                 | Lurbinectedin + atezolizumab |                                                                                                       | Atezolizumab       |                                                                                                       | Lurbinectedin + atezolizumab vs.<br>atezolizumab |
|---------------------------------------|------------------------------|-------------------------------------------------------------------------------------------------------|--------------------|-------------------------------------------------------------------------------------------------------|--------------------------------------------------|
|                                       | N/N <sup>Cen</sup>           | Median time to event in<br>days <sup>a</sup><br>[95% CI] <sup>b</sup><br>patients with event<br>n (%) | N/N <sup>Cen</sup> | Median time to event in<br>days <sup>a</sup><br>[95% CI] <sup>b</sup><br>patients with event<br>n (%) | HR [95% CI] <sup>c</sup><br>p-value <sup>d</sup> |
| Lymphocyte<br>count decreased         | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                                | NE [0.000; NE]<br>0.3183                         |
| Neutrophil count<br>decreased         | 242/239                      | NE [NE; NE]<br>3 (1.2)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                                | NE [0.000; NE]<br>0.0835                         |
| Platelet count<br>decreased           | 242/237                      | NE [NE; NE]<br>5 (2.1)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                                | NE [0.000; NE]<br>0.0370                         |
| White blood cell<br>count decreased   | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                                | NE [0.000; NE]<br>0.3183                         |
| Metabolism and<br>nutrition disorders | 242/237                      | NE [NE; NE]<br>5 (2.1)                                                                                | 240/237            | NE [NE; NE]<br>3 (1.3)                                                                                | 1.436 [0.340; 6.058]<br>0.6205                   |
| Acidosis                              | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                                | NE [0.000; NE]<br>0.3260                         |
| Alkalosis                             | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                                | NE [0.000; NE]<br>0.3258                         |
| Diabetic<br>ketoacidosis              | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                                | NE [0.000; NE]<br>0.3194                         |
| Hypocalcemia                          | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                                | NE [0.000; NE]<br>0.4752                         |

| Endpoint<br>SOC<br>PT                                                        | Lurbinectedin + atezolizumab |                                                                                                       | Atezolizumab       |                                                                                                       | Lurbinectedin + atezolizumab vs.<br>atezolizumab |
|------------------------------------------------------------------------------|------------------------------|-------------------------------------------------------------------------------------------------------|--------------------|-------------------------------------------------------------------------------------------------------|--------------------------------------------------|
|                                                                              | N/N <sup>Cen</sup>           | Median time to event in<br>days <sup>a</sup><br>[95% CI] <sup>b</sup><br>patients with event<br>n (%) | N/N <sup>Cen</sup> | Median time to event in<br>days <sup>a</sup><br>[95% CI] <sup>b</sup><br>patients with event<br>n (%) | HR [95% CI] <sup>c</sup><br>p-value <sup>d</sup> |
| Hypokalemia                                                                  | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                                | NE [0.000; NE]<br>0.4752                         |
| Hyponatremia                                                                 | 242/240                      | NE [NE; NE]<br>2 (0.8)                                                                                | 240/237            | NE [NE; NE]<br>3 (1.3)                                                                                | 0.592 [0.098; 3.570]<br>0.5635                   |
| Musculoskeletal<br>and connective<br>tissue disorders                        | 242/238                      | NE [NE; NE]<br>4 (1.7)                                                                                | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                                | 3.248 [0.359; 29.428]<br>0.2683                  |
| Arthralgia                                                                   | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                                | NE [0.000; NE]<br>0.4752                         |
| Back pain                                                                    | 242/240                      | NE [NE; NE]<br>2 (0.8)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                                | NE [0.000; NE]<br>0.1586                         |
| Mobility<br>decreased                                                        | 242/242                      | NE [NE; NE]<br>0 (0.0)                                                                                | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                                | 0.000 [0.000; NE]<br>0.3132                      |
| Pain in extremity                                                            | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                                | NE [0.000; NE]<br>0.4281                         |
| Neoplasms benign,<br>malignant and<br>unspecified (incl<br>cysts and polyps) | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                                | 0.736 [0.046; 11.848]<br>0.8281                  |
| Acute myeloid<br>leukemia                                                    | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                                | NE [0.000; NE]<br>0.4142                         |

| Endpoint<br>SOC<br>PT    | Lurbinectedin + atezolizumab |                                                                                                       | Atezolizumab       |                                                                                                       | Lurbinectedin + atezolizumab vs.<br>atezolizumab |
|--------------------------|------------------------------|-------------------------------------------------------------------------------------------------------|--------------------|-------------------------------------------------------------------------------------------------------|--------------------------------------------------|
|                          | N/N <sup>Cen</sup>           | Median time to event in<br>days <sup>a</sup><br>[95% CI] <sup>b</sup><br>patients with event<br>n (%) | N/N <sup>Cen</sup> | Median time to event in<br>days <sup>a</sup><br>[95% CI] <sup>b</sup><br>patients with event<br>n (%) | HR [95% CI] <sup>c</sup><br>p-value <sup>d</sup> |
| Prostate cancer          | 242/242                      | NE [NE; NE]<br>0 (0.0)                                                                                | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                                | 0.000 [0.000; NE]<br>0.2774                      |
| Nervous system disorders | 242/236                      | NE [NE; NE]<br>6 (2.5)                                                                                | 240/234            | NE [NE; NE]<br>6 (2.5)                                                                                | 0.690 [0.220; 2.166]<br>0.5224                   |
| Cerebrovascular accident | 242/242                      | NE [NE; NE]<br>0 (0.0)                                                                                | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                                | 0.000 [0.000; NE]<br>0.3163                      |
| Dizziness                | 242/240                      | NE [NE; NE]<br>2 (0.8)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                                | NE [0.000; NE]<br>0.2861                         |
| Nervous system disorder  | 242/242                      | NE [NE; NE]<br>0 (0.0)                                                                                | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                                | 0.000 [0.000; NE]<br>0.1717                      |
| Neuropathy peripheral    | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                                | 0.983 [0.061; 15.715]<br>0.9903                  |
| Seizure                  | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                                | 0.512 [0.032; 8.193]<br>0.6301                   |
| Spinal cord compression  | 242/242                      | NE [NE; NE]<br>0 (0.0)                                                                                | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                                | 0.000 [0.000; NE]<br>0.3086                      |
| Syncope                  | 242/240                      | NE [NE; NE]<br>2 (0.8)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                                | NE [0.000; NE]<br>0.2832                         |

| Endpoint<br>SOC<br>PT            | Lurbinectedin + atezolizumab |                                                                                                       | Atezolizumab       |                                                                                                       | Lurbinectedin + atezolizumab vs.<br>atezolizumab |
|----------------------------------|------------------------------|-------------------------------------------------------------------------------------------------------|--------------------|-------------------------------------------------------------------------------------------------------|--------------------------------------------------|
|                                  | N/N <sup>Cen</sup>           | Median time to event in<br>days <sup>a</sup><br>[95% CI] <sup>b</sup><br>patients with event<br>n (%) | N/N <sup>Cen</sup> | Median time to event in<br>days <sup>a</sup><br>[95% CI] <sup>b</sup><br>patients with event<br>n (%) | HR [95% CI] <sup>c</sup><br>p-value <sup>d</sup> |
| Transient<br>ischemic attack     | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                                | 0.712 [0.043; 11.823]<br>0.8118                  |
| Psychiatric<br>disorders         | 242/240                      | NE [NE; NE]<br>2 (0.8)                                                                                | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                                | 1.284 [0.113; 14.563]<br>0.8399                  |
| Completed<br>suicide             | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                                | NE [0.000; NE]<br>0.4751                         |
| Confusional state                | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                                | NE [0.000; NE]<br>0.3204                         |
| Delirium                         | 242/242                      | NE [NE; NE]<br>0 (0.0)                                                                                | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                                | 0.000 [0.000; NE]<br>0.1621                      |
| Renal and urinary<br>disorders   | 242/235                      | NE [NE; NE]<br>7 (2.9)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                                | NE [0.000; NE]<br>0.0281                         |
| Acute kidney<br>injury           | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                                | NE [0.000; NE]<br>0.3822                         |
| Immune-<br>mediated<br>nephritis | 242/240                      | NE [NE; NE]<br>2 (0.8)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                                | NE [0.000; NE]<br>0.2882                         |
| Nephropathy                      | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                                | NE [0.000; NE]<br>0.3183                         |

| Endpoint<br>SOC<br>PT                                    | Lurbinectedin + atezolizumab |                                                                                                       | Atezolizumab       |                                                                                                       | Lurbinectedin + atezolizumab vs.<br>atezolizumab |
|----------------------------------------------------------|------------------------------|-------------------------------------------------------------------------------------------------------|--------------------|-------------------------------------------------------------------------------------------------------|--------------------------------------------------|
|                                                          | N/N <sup>Cen</sup>           | Median time to event in<br>days <sup>a</sup><br>[95% CI] <sup>b</sup><br>patients with event<br>n (%) | N/N <sup>Cen</sup> | Median time to event in<br>days <sup>a</sup><br>[95% CI] <sup>b</sup><br>patients with event<br>n (%) | HR [95% CI] <sup>c</sup><br>p-value <sup>d</sup> |
| Perinephric<br>collection                                | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                                | NE [0.000; NE]<br>0.4734                         |
| Renal failure                                            | 242/239                      | NE [NE; NE]<br>3 (1.2)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                                | NE [0.000; NE]<br>0.1566                         |
| Respiratory,<br>thoracic and<br>mediastinal<br>disorders | 242/227                      | NE [NE; NE]<br>15 (6.2)                                                                               | 240/233            | NE [NE; NE]<br>7 (2.9)                                                                                | 1.871 [0.759; 4.612]<br>0.1669                   |
| Asthma                                                   | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                                | NE [0.000; NE]<br>0.3193                         |
| Bronchospasm                                             | 242/242                      | NE [NE; NE]<br>0 (0.0)                                                                                | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                                | 0.000 [0.000; NE]<br>0.3163                      |
| Dyspnea                                                  | 242/237                      | NE [NE; NE]<br>5 (2.1)                                                                                | 240/236            | NE [NE; NE]<br>4 (1.7)                                                                                | 1.076 [0.286; 4.051]<br>0.9140                   |
| Hemoptysis                                               | 242/240                      | NE [NE; NE]<br>2 (0.8)                                                                                | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                                | 1.714 [0.154; 19.127]<br>0.6576                  |
| Hypoxia                                                  | 242/242                      | NE [NE; NE]<br>0 (0.0)                                                                                | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                                | 0.000 [0.000; NE]<br>0.1714                      |
| Immune-<br>mediated lung<br>disease                      | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                                | NE [0.000; NE]<br>0.3193                         |

| Endpoint<br>SOC<br>PT                        | Lurbinectedin + atezolizumab |                                                                                                       | Atezolizumab       |                                                                                                       | Lurbinectedin + atezolizumab vs.<br>atezolizumab |
|----------------------------------------------|------------------------------|-------------------------------------------------------------------------------------------------------|--------------------|-------------------------------------------------------------------------------------------------------|--------------------------------------------------|
|                                              | N/N <sup>Cen</sup>           | Median time to event in<br>days <sup>a</sup><br>[95% CI] <sup>b</sup><br>patients with event<br>n (%) | N/N <sup>Cen</sup> | Median time to event in<br>days <sup>a</sup><br>[95% CI] <sup>b</sup><br>patients with event<br>n (%) | HR [95% CI] <sup>c</sup><br>p-value <sup>d</sup> |
| Pleural effusion                             | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                                | NE [0.000; NE]<br>0.3579                         |
| Pneumonitis                                  | 242/239                      | NE [NE; NE]<br>3 (1.2)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                                | NE [0.000; NE]<br>0.0901                         |
| Productive cough                             | 242/242                      | NE [NE; NE]<br>0 (0.0)                                                                                | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                                | 0.000 [0.000; NE]<br>0.1573                      |
| Pulmonary<br>embolism                        | 242/239                      | NE [NE; NE]<br>3 (1.2)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                                | NE [0.000; NE]<br>0.1245                         |
| Respiratory<br>failure                       | 242/240                      | NE [NE; NE]<br>2 (0.8)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                                | NE [0.000; NE]<br>0.1623                         |
| Skin and<br>subcutaneous tissue<br>disorders | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                                | NE [0.000; NE]<br>0.3237                         |
| Panniculitis                                 | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                                | NE [0.000; NE]<br>0.3237                         |
| Vascular disorders                           | 242/237                      | NE [NE; NE]<br>5 (2.1)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                                | NE [0.000; NE]<br>0.0480                         |
| Arteriosclerosis                             | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                                | NE [0.000; NE]<br>0.4334                         |

| Endpoint<br>SOC<br>PT                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         | Lurbinectedin + atezolizumab |                                                                                                       | Atezolizumab       |                                                                                                       | Lurbinectedin + atezolizumab vs.<br>atezolizumab |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------|-------------------------------------------------------------------------------------------------------|--------------------|-------------------------------------------------------------------------------------------------------|--------------------------------------------------|
|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               | N/N <sup>Cen</sup>           | Median time to event in<br>days <sup>a</sup><br>[95% CI] <sup>b</sup><br>patients with event<br>n (%) | N/N <sup>Cen</sup> | Median time to event in<br>days <sup>a</sup><br>[95% CI] <sup>b</sup><br>patients with event<br>n (%) | HR [95% CI] <sup>c</sup><br>p-value <sup>d</sup> |
| Hypotension                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                                | NE [0.000; NE]<br>0.4386                         |
| Superior vena<br>cava syndrome                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                                | NE [0.000; NE]<br>0.3843                         |
| Thrombophlebitis                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                                | NE [0.000; NE]<br>0.3313                         |
| Thrombosis                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                                | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                                | NE [0.000; NE]<br>0.3194                         |
| CCOD: 12 February 2025; NE: not estimable.<br>a: summaries of duration (median) are Kaplan-Meier estimates.<br>b: 95% CIs for the median were computed using the method of Brookmeyer and Crowley.<br>c: hazard ratios were estimated using a stratified Cox proportional hazard model. The stratification factors are ECOG PS at randomization (0 vs. 1), LDH at randomization ( $\leq$ ULN vs $>$ ULN) via local laboratory test, presence of liver metastases at enrollment (yes vs. no), and prior receipt of PCI (yes vs. no).<br>d: p-value based on the log rank test. |                              |                                                                                                       |                    |                                                                                                       |                                                  |

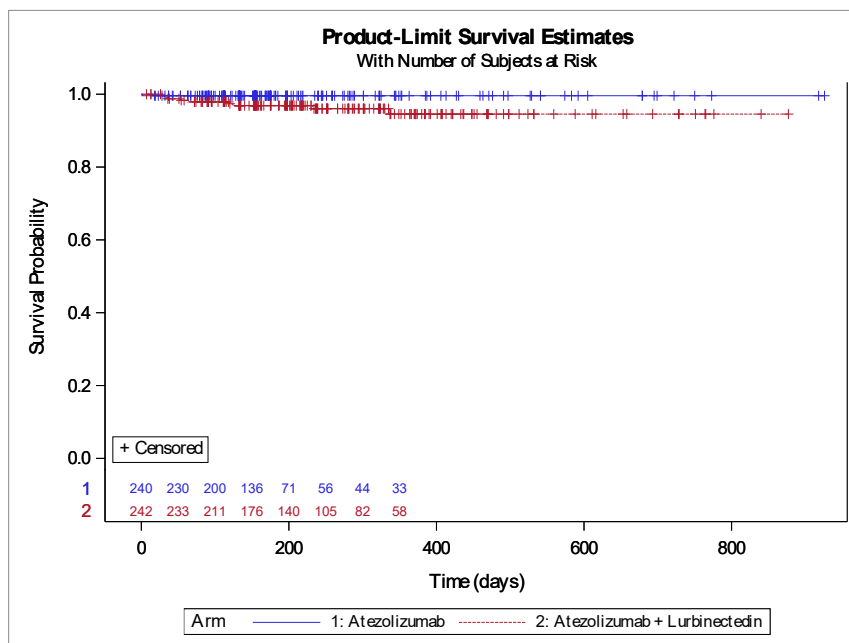


Abbildung 141: Kaplan-Meier plot for serious AE (SOC blood and lymphatic system disorders), IMforte trial, Safety Analysis Set, CCOD 12 February 2025

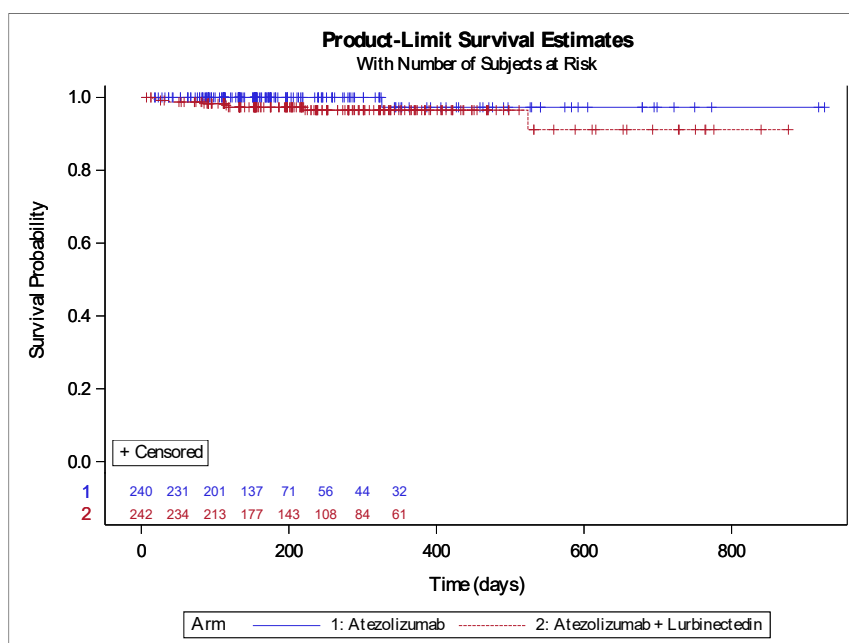


Abbildung 142: Kaplan-Meier plot for serious AE (SOC cardiac disorders), IMforte trial, Safety Analysis Set, CCOD 12 February 2025

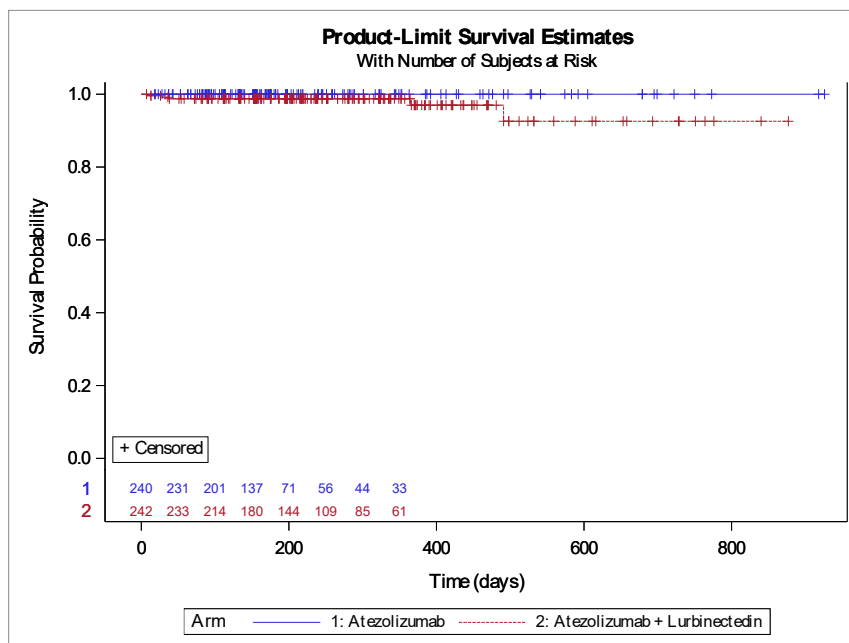


Abbildung 143: Kaplan-Meier plot for serious AE (PT platelet count decreased), IMforte trial, Safety Analysis Set, CCOD 12 February 2025

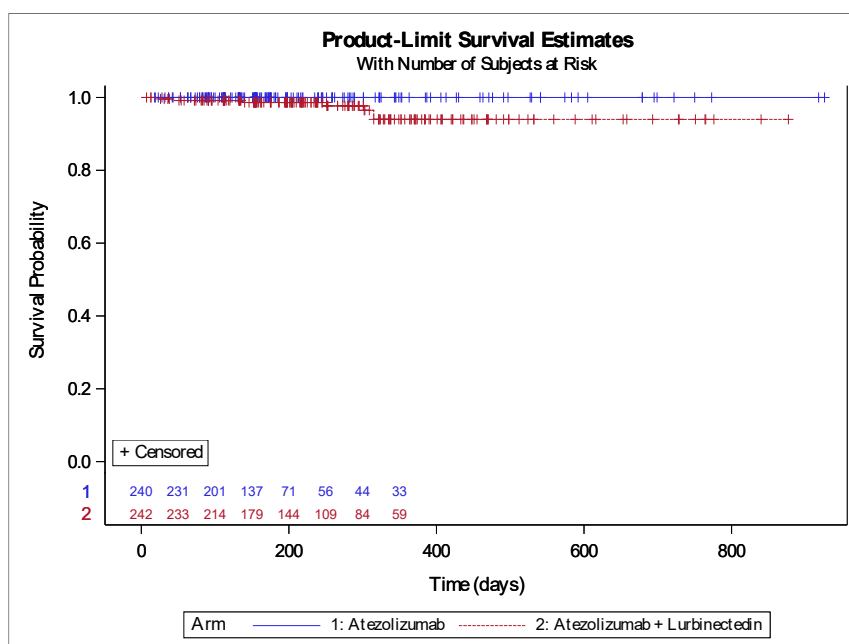


Abbildung 144: Kaplan-Meier plot for serious AE (SOC renal and urinary disorders), IMforte trial, Safety Analysis Set, CCOD 12 February 2025

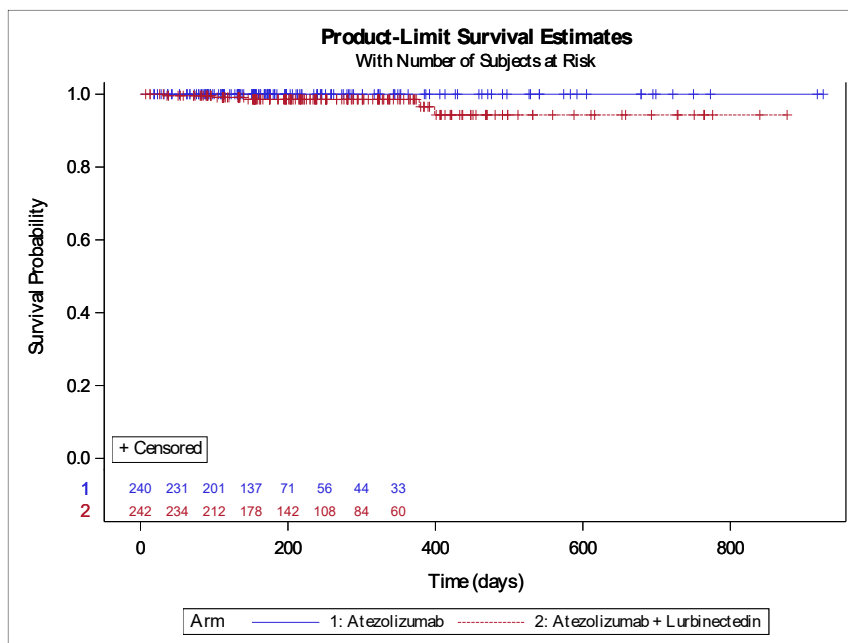


Abbildung 145: Kaplan-Meier plot for serious AE (SOC vascular disorders), IMforte trial, Safety Analysis Set, CCOD 12 February 2025

Tabelle 14: Treatment discontinuation due to AE by SOC and PT including effect estimates

| Endpoint<br>SOC<br>PT                                | Lurbinectedin + atezolizumab |                                                                                                    | Atezolizumab       |                                                                                                    | Lurbinectedin + atezolizumab vs. atezolizumab    |
|------------------------------------------------------|------------------------------|----------------------------------------------------------------------------------------------------|--------------------|----------------------------------------------------------------------------------------------------|--------------------------------------------------|
|                                                      | N/N <sup>Cen</sup>           | Median time to event in days <sup>a</sup><br>[95% CI] <sup>b</sup><br>patients with event<br>n (%) | N/N <sup>Cen</sup> | Median time to event in days <sup>a</sup><br>[95% CI] <sup>b</sup><br>patients with event<br>n (%) | HR [95% CI] <sup>c</sup><br>p-value <sup>d</sup> |
| Blood and lymphatic system disorders                 | 242/238                      | NE [NE; NE]<br>4 (1.7)                                                                             | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [0.000; NE]<br>0.0745                         |
| Anemia                                               | 242/239                      | NE [NE; NE]<br>3 (1.2)                                                                             | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [0.000; NE]<br>0.1070                         |
| Neutropenia                                          | 242/240                      | NE [NE; NE]<br>2 (0.8)                                                                             | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [0.000; NE]<br>0.2703                         |
| Thrombocytopenia                                     | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                             | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [0.000; NE]<br>0.4334                         |
| Gastrointestinal disorders                           | 242/240                      | NE [NE; NE]<br>2 (0.8)                                                                             | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                             | 1.980 [0.180; 21.833]<br>0.5696                  |
| Gastrointestinal hemorrhage                          | 242/242                      | NE [NE; NE]<br>0 (0.0)                                                                             | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                             | 0.000 [0.000; NE]<br>0.3110                      |
| Nausea                                               | 242/240                      | NE [NE; NE]<br>2 (0.8)                                                                             | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [0.000; NE]<br>0.1586                         |
| General disorders and administration site conditions | 242/239                      | NE [NE; NE]<br>3 (1.2)                                                                             | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [0.000; NE]<br>0.0848                         |

| Endpoint<br>SOC<br>PT                | Lurbinectedin + atezolizumab |                                                                                                    | Atezolizumab       |                                                                                                    | Lurbinectedin + atezolizumab vs. atezolizumab    |
|--------------------------------------|------------------------------|----------------------------------------------------------------------------------------------------|--------------------|----------------------------------------------------------------------------------------------------|--------------------------------------------------|
|                                      | N/N <sup>Cen</sup>           | Median time to event in days <sup>a</sup><br>[95% CI] <sup>b</sup><br>patients with event<br>n (%) | N/N <sup>Cen</sup> | Median time to event in days <sup>a</sup><br>[95% CI] <sup>b</sup><br>patients with event<br>n (%) | HR [95% CI] <sup>c</sup><br>p-value <sup>d</sup> |
| Fatigue                              | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                             | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [0.000; NE]<br>0.3193                         |
| Malaise                              | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                             | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [0.000; NE]<br>0.3193                         |
| Peripheral swelling                  | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                             | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [0.000; NE]<br>0.3237                         |
| Infections and infestations          | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                             | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                             | 0.927 [0.058; 14.851]<br>0.9575                  |
| Encephalitis                         | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                             | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [0.000; NE]<br>0.3527                         |
| Pneumonia                            | 242/242                      | NE [NE; NE]<br>0 (0.0)                                                                             | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                             | 0.000 [0.000; NE]<br>0.3163                      |
| Investigations                       | 242/239                      | NE [NE; NE]<br>3 (1.2)                                                                             | 240/238            | NE [NE; NE]<br>2 (0.8)                                                                             | 1.003 [0.164; 6.151]<br>0.9974                   |
| Blood alkaline phosphatase increased | 242/242                      | NE [NE; NE]<br>0 (0.0)                                                                             | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                             | 0.000 [0.000; NE]<br>0.1573                      |
| Blood creatinine increased           | 242/242                      | NE [NE; NE]<br>0 (0.0)                                                                             | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                             | 0.000 [0.000; NE]<br>0.1552                      |

| Endpoint<br>SOC<br>PT                           | Lurbinectedin + atezolizumab |                                                                                                    | Atezolizumab       |                                                                                                    | Lurbinectedin + atezolizumab vs. atezolizumab    |
|-------------------------------------------------|------------------------------|----------------------------------------------------------------------------------------------------|--------------------|----------------------------------------------------------------------------------------------------|--------------------------------------------------|
|                                                 | N/N <sup>Cen</sup>           | Median time to event in days <sup>a</sup><br>[95% CI] <sup>b</sup><br>patients with event<br>n (%) | N/N <sup>Cen</sup> | Median time to event in days <sup>a</sup><br>[95% CI] <sup>b</sup><br>patients with event<br>n (%) | HR [95% CI] <sup>c</sup><br>p-value <sup>d</sup> |
| Neutrophil count decreased                      | 242/239                      | NE [NE; NE]<br>3 (1.2)                                                                             | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [0.000; NE]<br>0.1154                         |
| Platelet count decreased                        | 242/240                      | NE [NE; NE]<br>2 (0.8)                                                                             | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [0.000; NE]<br>0.2176                         |
| White blood cell count decreased                | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                             | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [0.000; NE]<br>0.4685                         |
| Musculoskeletal and connective tissue disorders | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                             | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                             | 0.870 [0.054; 13.964]<br>0.9216                  |
| Joint swelling                                  | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                             | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [0.000; NE]<br>0.3237                         |
| Psoriatic arthropathy                           | 242/242                      | NE [NE; NE]<br>0 (0.0)                                                                             | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                             | 0.000 [0.000; NE]<br>0.2554                      |
| Nervous system disorders                        | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                             | 240/236            | NE [NE; NE]<br>4 (1.7)                                                                             | 0.169 [0.019; 1.538]<br>0.0749                   |
| Lethargy                                        | 242/242                      | NE [NE; NE]<br>0 (0.0)                                                                             | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                             | 0.000 [0.000; NE]<br>0.2254                      |
| Neuropathy peripheral                           | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                             | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                             | 0.983 [0.061; 15.715]<br>0.9903                  |

| Endpoint<br>SOC<br>PT                           | Lurbinectedin + atezolizumab |                                                                                                    | Atezolizumab       |                                                                                                    | Lurbinectedin + atezolizumab vs. atezolizumab    |
|-------------------------------------------------|------------------------------|----------------------------------------------------------------------------------------------------|--------------------|----------------------------------------------------------------------------------------------------|--------------------------------------------------|
|                                                 | N/N <sup>Cen</sup>           | Median time to event in days <sup>a</sup><br>[95% CI] <sup>b</sup><br>patients with event<br>n (%) | N/N <sup>Cen</sup> | Median time to event in days <sup>a</sup><br>[95% CI] <sup>b</sup><br>patients with event<br>n (%) | HR [95% CI] <sup>c</sup><br>p-value <sup>d</sup> |
| Peripheral motor neuropathy                     | 242/242                      | NE [NE; NE]<br>0 (0.0)                                                                             | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                             | 0.000 [0.000; NE]<br>0.1588                      |
| Peripheral sensory neuropathy                   | 242/242                      | NE [NE; NE]<br>0 (0.0)                                                                             | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                             | 0.000 [0.000; NE]<br>0.1588                      |
| Seizure                                         | 242/242                      | NE [NE; NE]<br>0 (0.0)                                                                             | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                             | 0.000 [0.000; NE]<br>0.1614                      |
| Trigeminal neuropathy                           | 242/242                      | NE [NE; NE]<br>0 (0.0)                                                                             | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                             | 0.000 [0.000; NE]<br>0.1588                      |
| Renal and urinary disorders                     | 242/239                      | NE [NE; NE]<br>3 (1.2)                                                                             | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [0.000; NE]<br>0.1282                         |
| Immune-mediated nephritis                       | 242/240                      | NE [NE; NE]<br>2 (0.8)                                                                             | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [0.000; NE]<br>0.2478                         |
| Nephropathy                                     | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                             | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [0.000; NE]<br>0.3183                         |
| Respiratory, thoracic and mediastinal disorders | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                             | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                             | 0.727 [0.044; 12.013]<br>0.8228                  |
| Dyspnea                                         | 242/242                      | NE [NE; NE]<br>0 (0.0)                                                                             | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                             | 0.000 [0.000; NE]<br>0.1692                      |

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

| Endpoint<br>SOC<br>PT                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         | Lurbinectedin + atezolizumab |                                                                                                    | Atezolizumab       |                                                                                                    | Lurbinectedin + atezolizumab vs. atezolizumab    |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------|----------------------------------------------------------------------------------------------------|--------------------|----------------------------------------------------------------------------------------------------|--------------------------------------------------|
|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               | N/N <sup>Cen</sup>           | Median time to event in days <sup>a</sup><br>[95% CI] <sup>b</sup><br>patients with event<br>n (%) | N/N <sup>Cen</sup> | Median time to event in days <sup>a</sup><br>[95% CI] <sup>b</sup><br>patients with event<br>n (%) | HR [95% CI] <sup>c</sup><br>p-value <sup>d</sup> |
| Pneumonitis                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   | 242/241                      | NE [NE; NE]<br>1 (0.4)                                                                             | 240/239            | NE [NE; NE]<br>1 (0.4)                                                                             | 0.727 [0.044; 12.013]<br>0.8228                  |
| Vascular disorders                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            | 242/240                      | NE [NE; NE]<br>2 (0.8)                                                                             | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [0.000; NE]<br>0.1632                         |
| Phlebitis                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | 242/240                      | NE [NE; NE]<br>2 (0.8)                                                                             | 240/240            | NE [NE; NE]<br>0 (0.0)                                                                             | NE [0.000; NE]<br>0.1632                         |
| CCOD: 12 February 2025; NE: not estimable.<br>a: summaries of duration (median) are Kaplan-Meier estimates.<br>b: 95% CIs for the median were computed using the method of Brookmeyer and Crowley.<br>c: hazard ratios were estimated using a stratified Cox proportional hazard model. The stratification factors are ECOG PS at randomization (0 vs. 1), LDH at randomization ( $\leq$ ULN vs $>$ ULN) via local laboratory test, presence of liver metastases at enrollment (yes vs. no), and prior receipt of PCI (yes vs. no).<br>d: p-value based on the log rank test. |                              |                                                                                                    |                    |                                                                                                    |                                                  |

Tabelle 15: Subgroup analysis for safety endpoints (IMforte)

| Outcome<br>Subgroup             | Lurbinectedin + atezolizumab |                                                                                                       | Atezolizumab       |                                                                                                       | Lurbinectedin + atezolizumab vs. atezolizumab<br>HR [95% CI] <sup>c</sup><br>p-value <sup>d</sup> |
|---------------------------------|------------------------------|-------------------------------------------------------------------------------------------------------|--------------------|-------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------|
|                                 | N/N <sup>Cen</sup>           | Median time to event<br>in days <sup>a</sup><br>[95% CI] <sup>b</sup><br>patients with event<br>n (%) | N/N <sup>Cen</sup> | Median time to event<br>in days <sup>a</sup><br>[95% CI] <sup>b</sup><br>patients with event<br>n (%) |                                                                                                   |
| Time to first occurrence of AE  |                              |                                                                                                       |                    |                                                                                                       |                                                                                                   |
| Total AE                        |                              |                                                                                                       |                    |                                                                                                       |                                                                                                   |
| PCI                             |                              |                                                                                                       |                    |                                                                                                       |                                                                                                   |
| Yes                             | 34/0                         | 5.5 [2; 10]<br>34 (100.0)                                                                             | 37/4               | 35 [21; 65]<br>33 (89.2)                                                                              | 3.313 [1.907; 5.757]<br><.0001                                                                    |
| No                              | 208/7                        | 10 [9; 17]<br>201 (96.6)                                                                              | 203/40             | 35 [23; 42]<br>163 (80.3)                                                                             | 2.055 [1.659; 2.546]<br><.0001                                                                    |
| Response to induction treatment |                              |                                                                                                       |                    |                                                                                                       |                                                                                                   |
| PR/SD                           | 227/6                        | 10 [9; 11]<br>221 (97.4)                                                                              | 235/41             | 35 [23; 42]<br>194 (82.6)                                                                             | 2.155 [1.763; 2.636]<br><.0001                                                                    |
| CR                              | 7/0                          | 3 [2; 29]<br>7 (100.0)                                                                                | 2/1                | NE [12; NE]<br>1 (50.0)                                                                               | 3.473 [0.408; 29.586]<br>0.2274                                                                   |
| Severe AE Grade ≥3              |                              |                                                                                                       |                    |                                                                                                       |                                                                                                   |
| PCI                             |                              |                                                                                                       |                    |                                                                                                       |                                                                                                   |
| Yes                             | 34/15                        | 336 [39; 349]<br>19 (55.9)                                                                            | 37/24              | NE [205; NE]<br>13 (35.1)                                                                             | 1.865 [0.919; 3.787]<br>0.0797                                                                    |
| No                              | 208/115                      | 343 [254; 490]<br>93 (44.7)                                                                           | 203/151            | NE [326; NE]<br>52 (25.6)                                                                             | 1.654 [1.174; 2.330]<br>0.0036                                                                    |

| Outcome Subgroup                | Lurbinectedin + atezolizumab |                                                                                                       | Atezolizumab       |                                                                                                       | Lurbinectedin + atezolizumab vs. atezolizumab<br>HR [95% CI] <sup>c</sup><br>p-value <sup>d</sup> |
|---------------------------------|------------------------------|-------------------------------------------------------------------------------------------------------|--------------------|-------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------|
|                                 | N/N <sup>Cen</sup>           | Median time to event<br>in days <sup>a</sup><br>[95% CI] <sup>b</sup><br>patients with event<br>n (%) | N/N <sup>Cen</sup> | Median time to event<br>in days <sup>a</sup><br>[95% CI] <sup>b</sup><br>patients with event<br>n (%) |                                                                                                   |
| Response to induction treatment |                              |                                                                                                       |                    |                                                                                                       |                                                                                                   |
| PR/SD                           | 227/119                      | 304 [223; 403]<br>108 (47.6)                                                                          | 235/170            | NE [326; NE]<br>65 (27.7)                                                                             | 1.707 [1.252; 2.328]<br>0.0006                                                                    |
| CR                              | 7/3                          | 147 [11; NE]<br>4 (57.1)                                                                              | 2/2                | NE [NE; NE]<br>0 (0.0)                                                                                | NE [0.000; NE]<br>0.2604                                                                          |
| Grade 3 AE                      |                              |                                                                                                       |                    |                                                                                                       |                                                                                                   |
| PCI                             |                              |                                                                                                       |                    |                                                                                                       |                                                                                                   |
| Yes                             | 34/18                        | 343 [43; NE]<br>16 (47.1)                                                                             | 37/27              | NE [218; NE]<br>10 (27.0)                                                                             | 2.033 [0.920; 4.489]<br>0.0733                                                                    |
| No                              | 208/121                      | 393 [276; 545]<br>87 (41.8)                                                                           | 203/162            | NE [NE; NE]<br>41 (20.2)                                                                              | 1.975 [1.359; 2.871]<br>0.0003                                                                    |
| Response to induction treatment |                              |                                                                                                       |                    |                                                                                                       |                                                                                                   |
| PR/SD                           | 227/127                      | 343 [276; 442]<br>100 (44.1)                                                                          | 235/184            | NE [NE; NE]<br>51 (21.7)                                                                              | 2.020 [1.439; 2.837]<br><.0001                                                                    |
| CR                              | 7/4                          | NE [30; NE]<br>3 (42.9)                                                                               | 2/2                | NE [NE; NE]<br>0 (0.0)                                                                                | NE [0.000; NE]<br>0.3340                                                                          |
| Grade 4 AE                      |                              |                                                                                                       |                    |                                                                                                       |                                                                                                   |
| PCI                             |                              |                                                                                                       |                    |                                                                                                       |                                                                                                   |
| Yes                             | 34/27                        | NE [NE; NE]<br>7 (20.6)                                                                               | 37/35              | NE [NE; NE]<br>2 (5.4)                                                                                | 3.993 [0.826; 19.294]<br>0.0627                                                                   |
| No                              | 208/186                      | NE [NE; NE]<br>22 (10.6)                                                                              | 203/193            | NE [NE; NE]<br>10 (4.9)                                                                               | 1.865 [0.878; 3.963]<br>0.0997                                                                    |
| Response to induction treatment |                              |                                                                                                       |                    |                                                                                                       |                                                                                                   |

| Outcome<br>Subgroup              | Lurbinectedin + atezolizumab |                                                                                                       | Atezolizumab       |                                                                                                       | Lurbinectedin + atezolizumab vs. atezolizumab<br><br>HR [95% CI] <sup>c</sup><br>p-value <sup>d</sup> |
|----------------------------------|------------------------------|-------------------------------------------------------------------------------------------------------|--------------------|-------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------|
|                                  | N/N <sup>Cen</sup>           | Median time to event<br>in days <sup>a</sup><br>[95% CI] <sup>b</sup><br>patients with event<br>n (%) | N/N <sup>Cen</sup> | Median time to event<br>in days <sup>a</sup><br>[95% CI] <sup>b</sup><br>patients with event<br>n (%) |                                                                                                       |
| PR/SD                            | 227/199                      | NE [NE; NE]<br>28 (12.3)                                                                              | 235/223            | NE [NE; NE]<br>12 (5.1)                                                                               | 2.213 [1.121; 4.368]<br>0.0188                                                                        |
| CR                               | 7/6                          | NE [NE; NE]<br>1 (14.3)                                                                               | 2/2                | NE [NE; NE]<br>0 (0.0)                                                                                | NE [0.000; NE]<br>0.5637                                                                              |
| Grade 5 AE (death related to AE) |                              |                                                                                                       |                    |                                                                                                       |                                                                                                       |
| PCI                              |                              |                                                                                                       |                    |                                                                                                       |                                                                                                       |
| Yes                              | 34/32                        | NE [NE; NE]<br>2 (5.9)                                                                                | 37/36              | NE [NE; NE]<br>1 (2.7)                                                                                | 1.914 [0.172; 21.266]<br>0.5907                                                                       |
| No                               | 208/198                      | NE [NE; NE]<br>10 (4.8)                                                                               | 203/198            | NE [NE; NE]<br>5 (2.5)                                                                                | 1.622 [0.549; 4.794]<br>0.3775                                                                        |
| Response to induction treatment  |                              |                                                                                                       |                    |                                                                                                       |                                                                                                       |
| PR/SD                            | 227/216                      | NE [NE; NE]<br>11 (4.8)                                                                               | 235/229            | NE [NE; NE]<br>6 (2.6)                                                                                | 1.603 [0.588; 4.369]<br>0.3523                                                                        |
| CR                               | 7/6                          | NE [NE; NE]<br>1 (14.3)                                                                               | 02. Feb            | NE [NE; NE]<br>0 (0.0)                                                                                | NE [0.000; NE]<br>0.5930                                                                              |
| Serious AE                       |                              |                                                                                                       |                    |                                                                                                       |                                                                                                       |
| PCI                              |                              |                                                                                                       |                    |                                                                                                       |                                                                                                       |
| Yes                              | 34/18                        | 287 [41; NE]<br>16 (47.1)                                                                             | 37/25              | NE [218; NE]<br>12 (32.4)                                                                             | 1.594 [0.752; 3.378]<br>0.2192                                                                        |
| No                               | 208/141                      | 512 [378; NE]<br>67 (32.2)                                                                            | 203/172            | NE [NE; NE]<br>31 (15.3)                                                                              | 1.852 [1.206; 2.844]<br>0.0042                                                                        |
| Response to induction treatment  |                              |                                                                                                       |                    |                                                                                                       |                                                                                                       |
| PR/SD                            | 227/146                      | 442 [348; NE]<br>81 (35.7)                                                                            | 235/192            | NE [NE; NE]<br>43 (18.3)                                                                              | 1.818 [1.253; 2.636]<br>0.0014                                                                        |

| Outcome<br>Subgroup                 | Lurbinectedin + atezolizumab |                                                                                                       | Atezolizumab       |                                                                                                       | Lurbinectedin + atezolizumab vs. atezolizumab<br><br>HR [95% CI] <sup>c</sup><br>p-value <sup>d</sup> |
|-------------------------------------|------------------------------|-------------------------------------------------------------------------------------------------------|--------------------|-------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------|
|                                     | N/N <sup>Cen</sup>           | Median time to event<br>in days <sup>a</sup><br>[95% CI] <sup>b</sup><br>patients with event<br>n (%) | N/N <sup>Cen</sup> | Median time to event<br>in days <sup>a</sup><br>[95% CI] <sup>b</sup><br>patients with event<br>n (%) |                                                                                                       |
| CR                                  | 7/6                          | NE [NE; NE]<br>1 (14.3)                                                                               | 2/2                | NE [NE; NE]<br>0 (0.0)                                                                                | NE [0.000; NE]<br>0.5930                                                                              |
| Treatment discontinuation due to AE |                              |                                                                                                       |                    |                                                                                                       |                                                                                                       |
| PCI                                 |                              |                                                                                                       |                    |                                                                                                       |                                                                                                       |
| Yes                                 | 34/30                        | NE [393; NE]<br>4 (11.8)                                                                              | 37/32              | NE [NE; NE]<br>5 (13.5)                                                                               | 0.761 [0.203; 2.855]<br>0.6843                                                                        |
| No                                  | 208/195                      | NE [NE; NE]<br>13 (6.3)                                                                               | 203/198            | NE [NE; NE]<br>5 (2.5)                                                                                | 2.240 [0.794; 6.322]<br>0.1178                                                                        |
| Response to induction treatment     |                              |                                                                                                       |                    |                                                                                                       |                                                                                                       |
| PR/SD                               | 227/210                      | NE [NE; NE]<br>17 (7.5)                                                                               | 235/225            | NE [NE; NE]<br>10 (4.3)                                                                               | 1.517 [0.691; 3.332]<br>0.2961                                                                        |
| CR                                  | 7/7                          | NE [NE; NE]<br>0 (0.0)                                                                                | 2/2                | NE [NE; NE]<br>0 (0.0)                                                                                | NE [NE; NE]<br>NE                                                                                     |
| Immune-related AE <sup>f</sup>      |                              |                                                                                                       |                    |                                                                                                       |                                                                                                       |
| PCI                                 |                              |                                                                                                       |                    |                                                                                                       |                                                                                                       |
| Yes                                 | 34/24                        | NE [260; NE]<br>10 (29.4)                                                                             | 37/26              | NE [253; NE]<br>11 (29.7)                                                                             | 0.727 [0.290; 1.825]<br>0.4954                                                                        |
| No                                  | 208/133                      | 353 [316; NE]<br>75 (36.1)                                                                            | 203/156            | NE [360; NE]<br>47 (23.2)                                                                             | 1.338 [0.910; 1.967]<br>0.1380                                                                        |
| Response to induction treatment     |                              |                                                                                                       |                    |                                                                                                       |                                                                                                       |
| PR/SD                               | 227/146                      | 444 [316; NE]<br>81 (35.7)                                                                            | 235/178            | NE [400; NE]<br>57 (24.3)                                                                             | 1.229 [0.859; 1.757]<br>0.2585                                                                        |
| CR                                  | 7/4                          | NE [23; NE]<br>3 (42.9)                                                                               | 2/1                | NE [41; NE]<br>1 (50.0)                                                                               | 1.057 [0.108; 10.322]<br>0.9622                                                                       |

| Outcome<br>Subgroup                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   | Lurbinectedin + atezolizumab |                                                                                                       | Atezolizumab       |                                                                                                       | Lurbinectedin + atezolizumab vs. atezolizumab    |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------|-------------------------------------------------------------------------------------------------------|--------------------|-------------------------------------------------------------------------------------------------------|--------------------------------------------------|
|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       | N/N <sup>Cen</sup>           | Median time to event<br>in days <sup>a</sup><br>[95% CI] <sup>b</sup><br>patients with event<br>n (%) | N/N <sup>Cen</sup> | Median time to event<br>in days <sup>a</sup><br>[95% CI] <sup>b</sup><br>patients with event<br>n (%) | HR [95% CI] <sup>c</sup><br>p-value <sup>d</sup> |
| <p>Reading the “Hypothesis testing” columns:</p> <p>1. Statistical significance: S = Statistically significant against the alpha level specified in the statistical analysis plan of the corresponding study, NS = Non-significant, NO = Nominal p-value</p> <p>2. Prespecification: P = Statistical test was prespecified according to the statistical analysis plan of the corresponding study, NP = Not prespecified</p> <p>3. Multiple hypothesis testing. C = Appropriate control for multiplicity according to the statistical analysis plan and clinical study report of the corresponding study, NC = Not controlled</p> <p>CCOD: 12 February 2025; NE: not estimable.</p> <p>a: summaries of duration (median) are Kaplan-Meier estimates.</p> <p>b: 95% CIs for the median were computed using the method of Brookmeyer and Crowley.</p> <p>c: hazard ratios were estimated using a stratified Cox proportional hazard model. The stratification factors are ECOG PS at randomization (0 vs. 1), LDH at randomization (<math>\leq</math>ULN vs <math>&gt;</math>ULN) via local laboratory test, presence of liver metastases at enrollment (yes vs. no), and prior receipt of PCI (yes vs. no).</p> <p>d: p-value based on the log rank test.</p> <p>e: quantile regression analysis.</p> <p>f: specific AE, as requested by the assessment scope. Immune-related AE were calculated as a combined endpoint comprising the following immune-mediated AE: adrenal insufficiency, colitis, diabetes mellitus, encephalitis, Guillain-Barre syndrome, hepatitis (diagnosis and lab abnormalities), hepatitis (diagnosis), hepatitis (lab abnormalities), hyperthyroidism, hypothyroidism, meningoencephalitis, myositis, myositis (myositis + rhabdomyolysis) nephritis, ocular inflammatory toxicity, pancreatitis, pericardial disorders, pneumonitis, rhabdomyolysis, rash, severe cutaneous reactions, and vasculitis.</p> |                              |                                                                                                       |                    |                                                                                                       |                                                  |

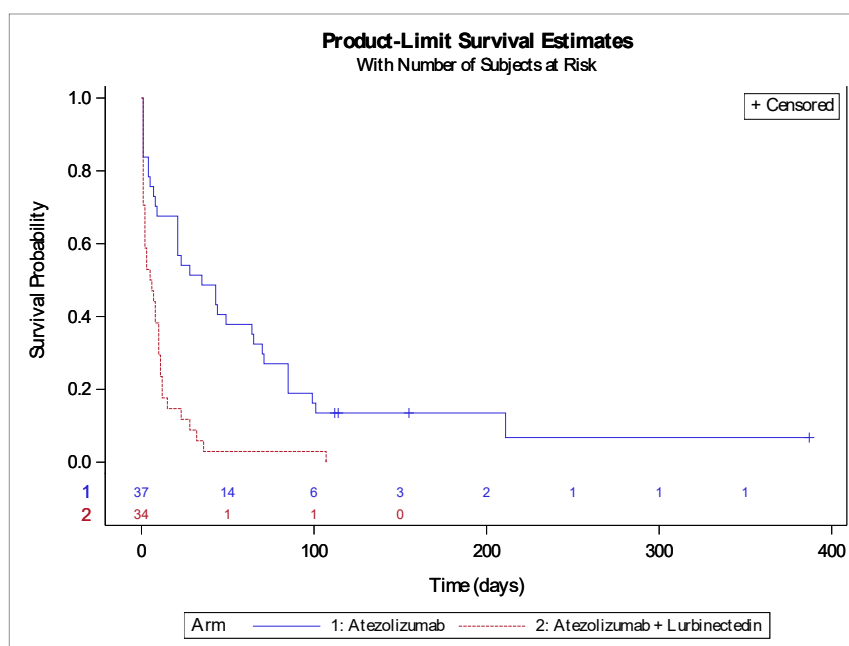


Abbildung 146: Kaplan-Meier plot for any AE, patients receiving PCI prior to randomization, IMforte trial, Safety Analysis Set, CCOD 12 February 2025

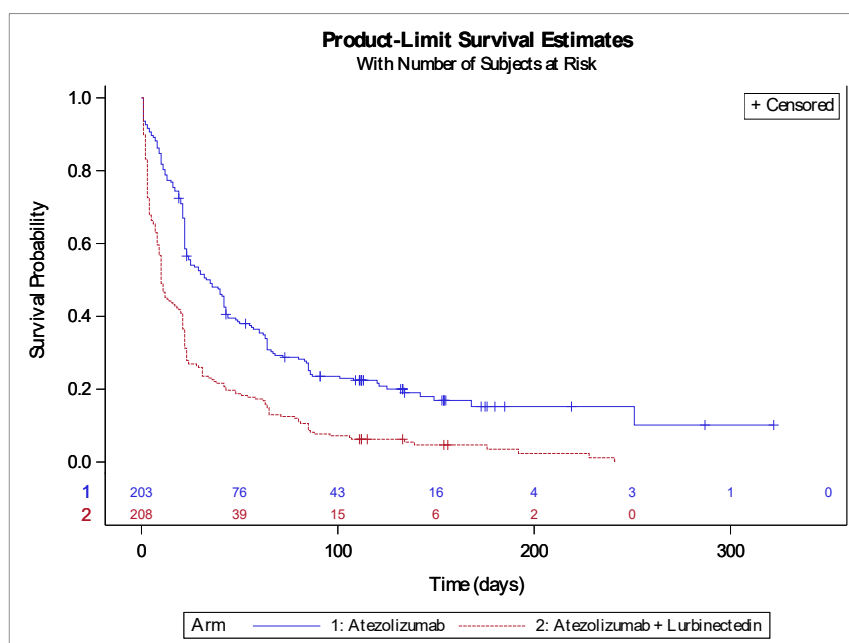


Abbildung 147: Kaplan-Meier plot for any AE, patients not receiving PCI prior to randomization, IMforte trial, Safety Analysis Set, CCOD 12 February 2025

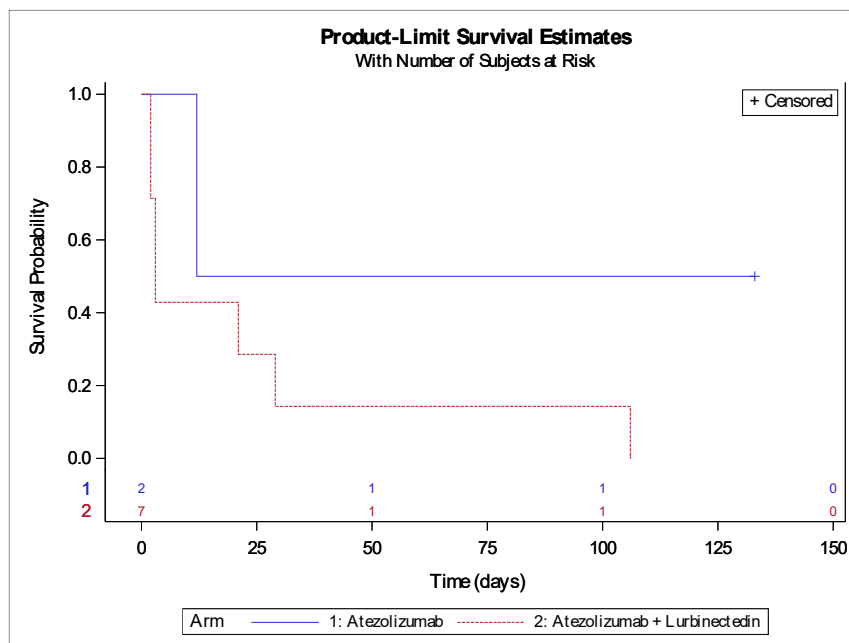


Abbildung 148: Kaplan-Meier plot for any AE, patients with CR to induction treatment, IMforte trial, Safety Analysis Set, CCOD 12 February 2025

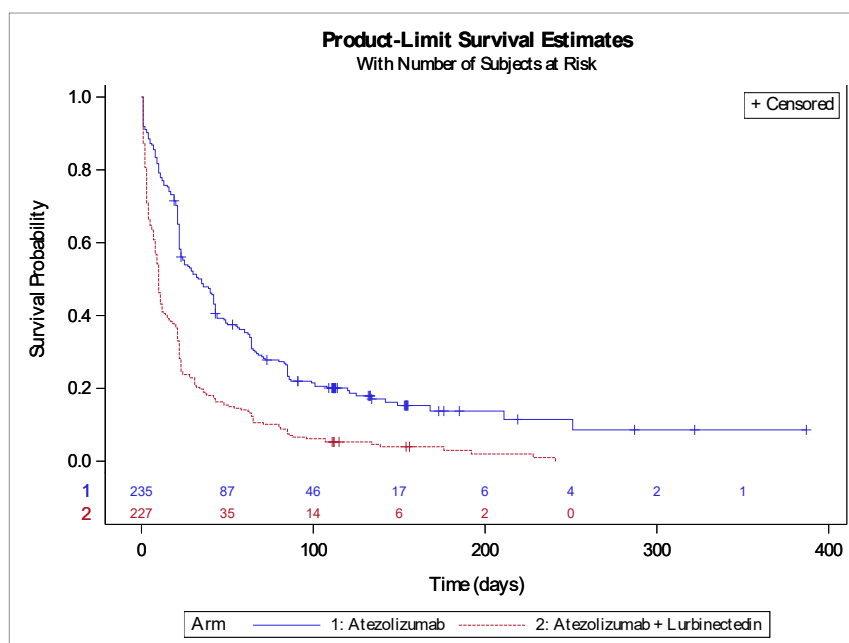


Abbildung 149: Kaplan-Meier plot for any AE, patients with PR/SD to induction treatment, IMforte trial, Safety Analysis Set, CCOD 12 February 2025

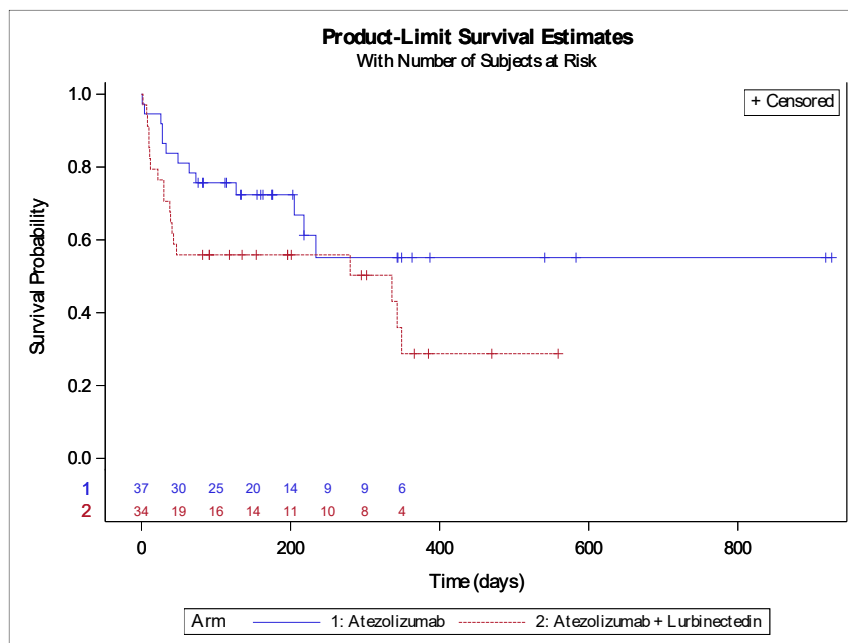


Abbildung 150: Kaplan-Meier plot for severe AE (grade  $\geq 3$ ), patients receiving PCI prior to randomization, IMforte trial, Safety Analysis Set, CCOD 12 February 2025

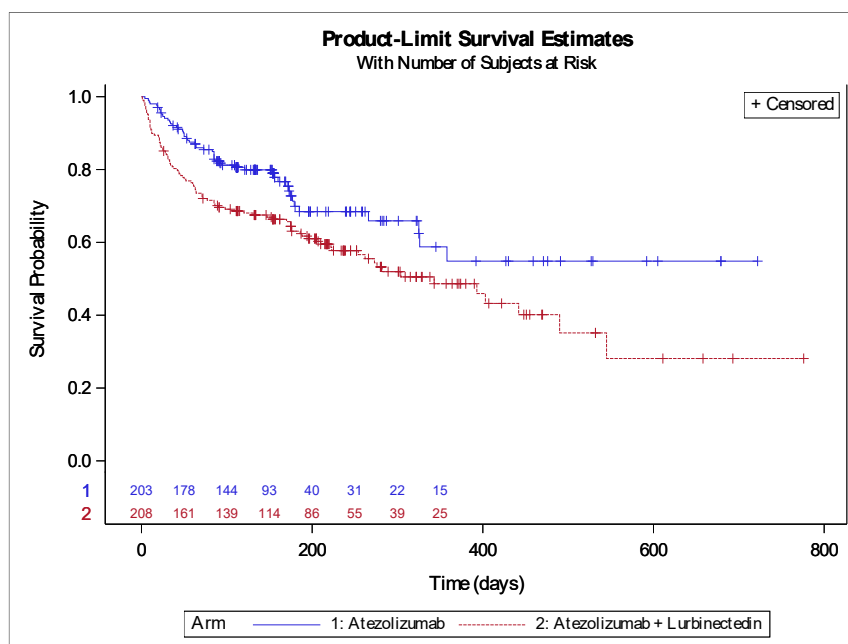


Abbildung 151: Kaplan-Meier plot for severe AE (grade  $\geq 3$ ), patients not receiving PCI prior to randomization, IMforte trial, Safety Analysis Set, CCOD 12 February 2025

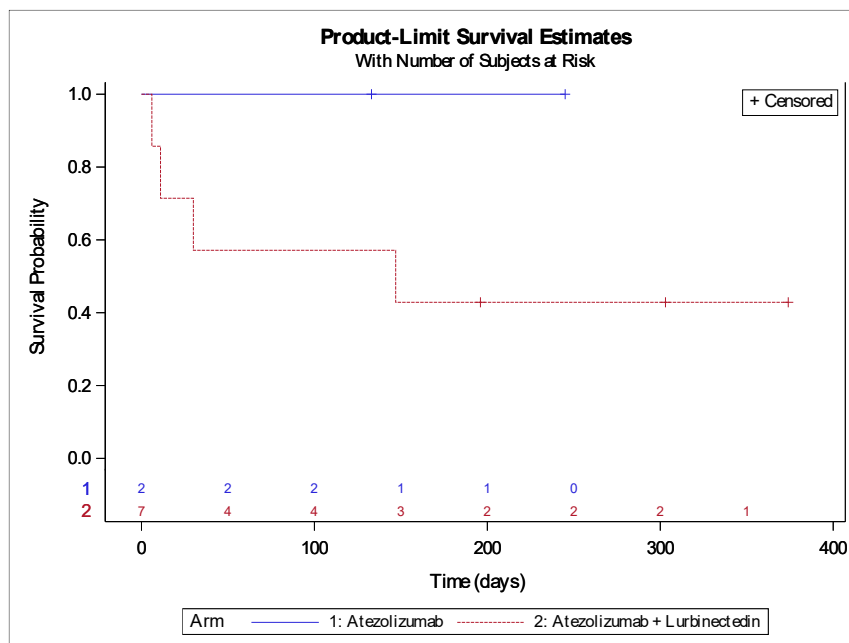


Abbildung 152: Kaplan-Meier plot for severe AE (grade  $\geq 3$ ), patients with CR to induction treatment, IMforte trial, Safety Analysis Set, CCOD 12 February 2025

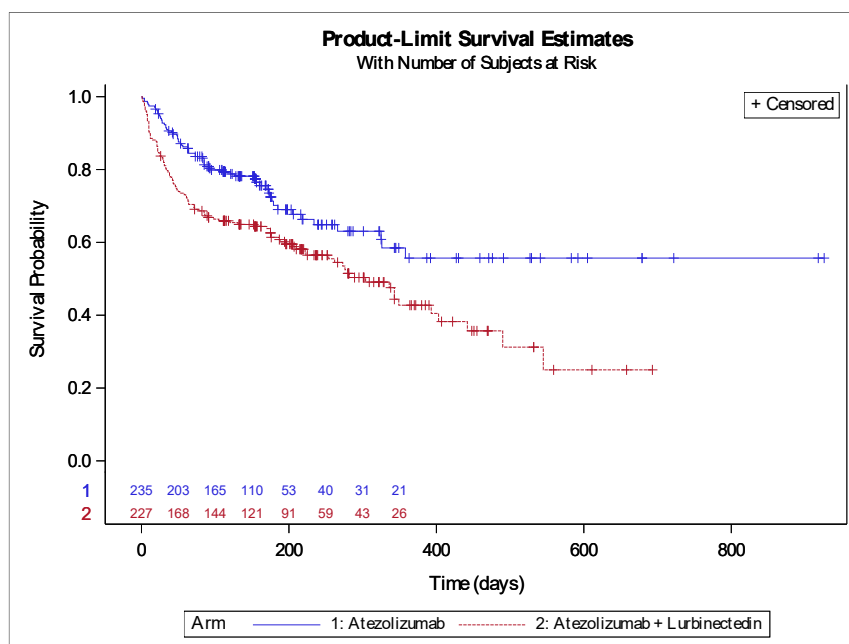


Abbildung 153: Kaplan-Meier plot for severe AE (grade  $\geq 3$ ), patients with PR/SD to induction treatment, IMforte trial, Safety Analysis Set, CCOD 12 February 2025

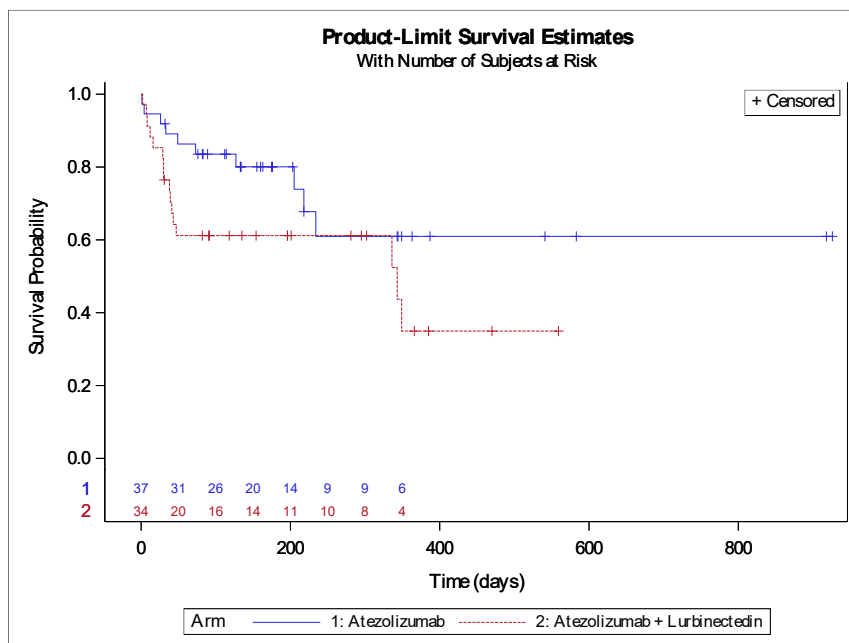


Abbildung 154: Kaplan-Meier plot for AE grade 3, patients receiving PCI prior to randomization, IMforte trial, Safety Analysis Set, CCOD 12 February 2025

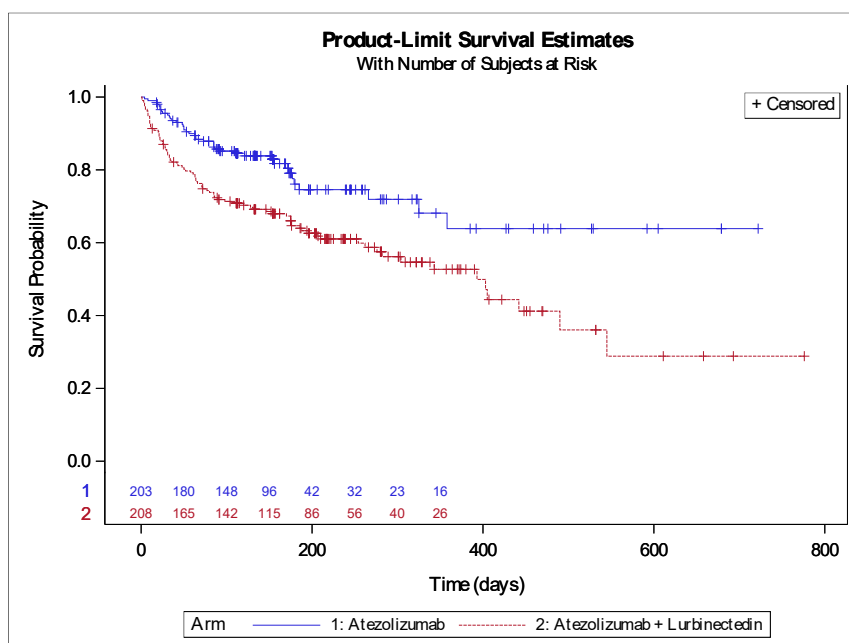


Abbildung 155: Kaplan-Meier plot for AE grade 3, patients not receiving PCI prior to randomization, IMforte trial, Safety Analysis Set, CCOD 12 February 2025

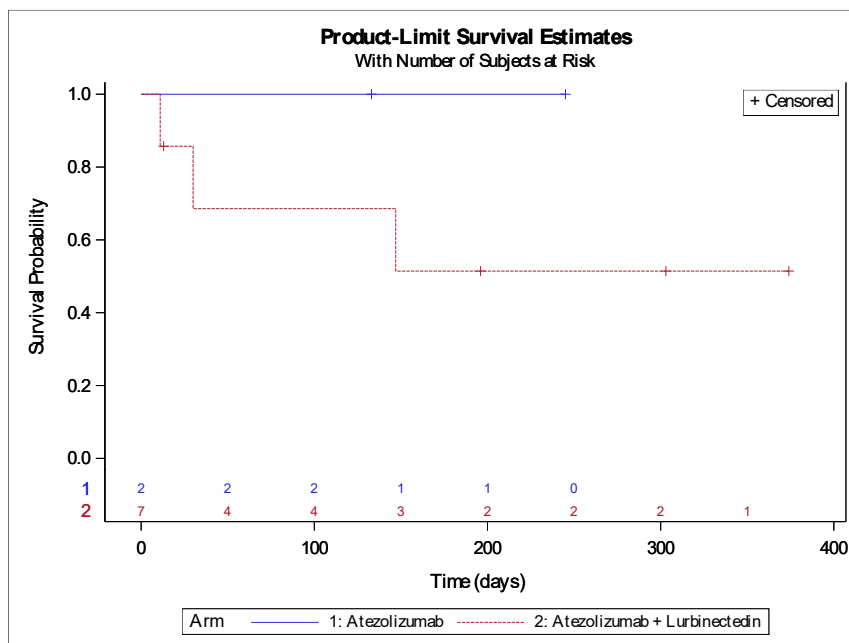


Abbildung 156: Kaplan-Meier plot for AE grade 3, patients with CR to induction treatment, IMforte trial, Safety Analysis Set, CCOD 12 February 2025

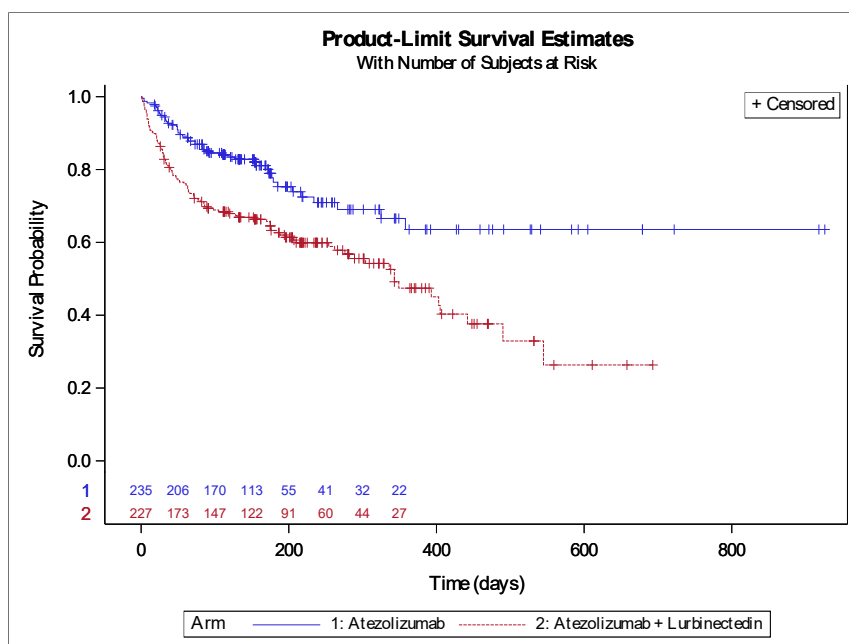


Abbildung 157: Kaplan-Meier plot for AE grade 3, patients with PR/SD to induction treatment, IMforte trial, Safety Analysis Set, CCOD 12 February 2025

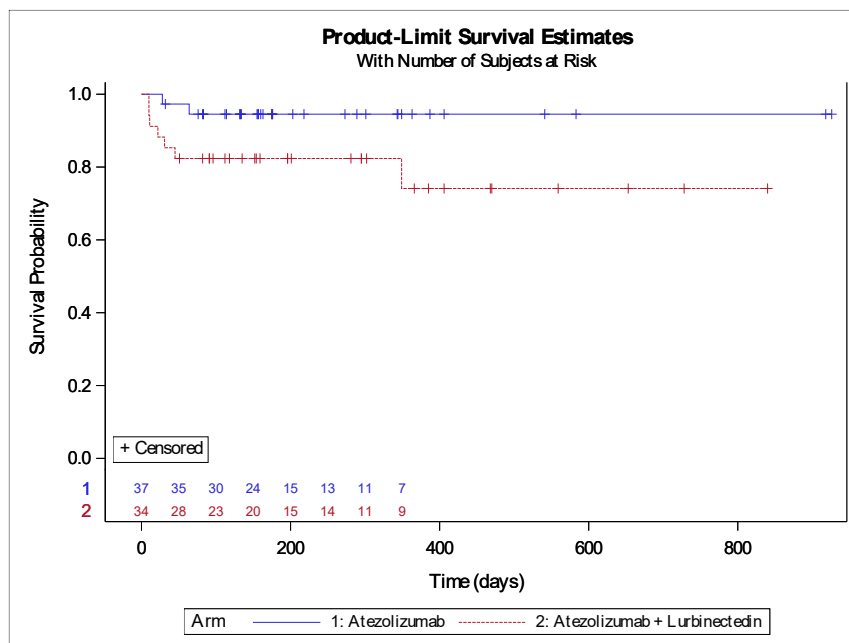


Abbildung 158: Kaplan-Meier plot for AE grade 4, patients receiving PCI prior to randomization, IMforte trial, Safety Analysis Set, CCOD 12 February 2025

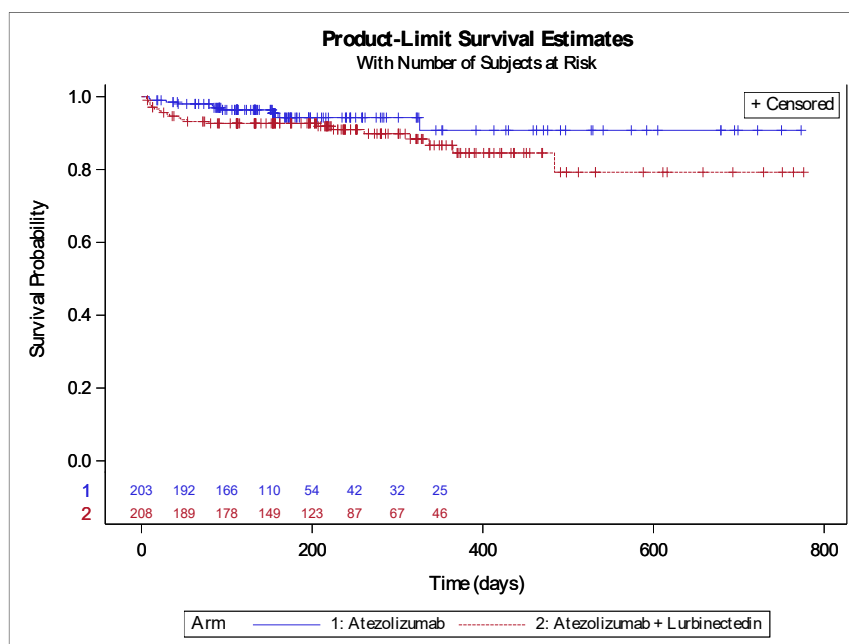


Abbildung 159: Kaplan-Meier plot for AE grade 4, patients not receiving PCI prior to randomization, IMforte trial, Safety Analysis Set, CCOD 12 February 2025

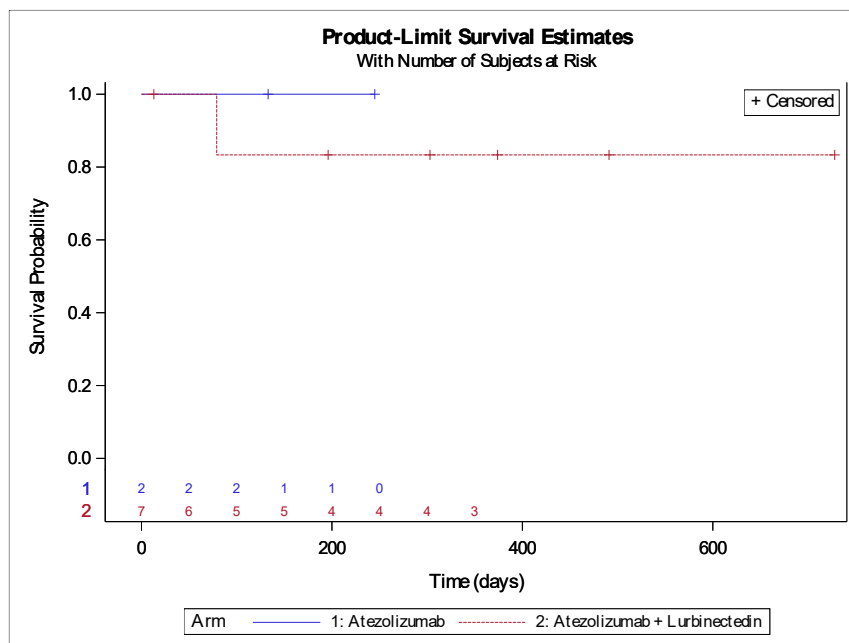


Abbildung 160: Kaplan-Meier plot for AE grade 4, patients with CR to induction treatment, IMforte trial, Safety Analysis Set, CCOD 12 February 2025

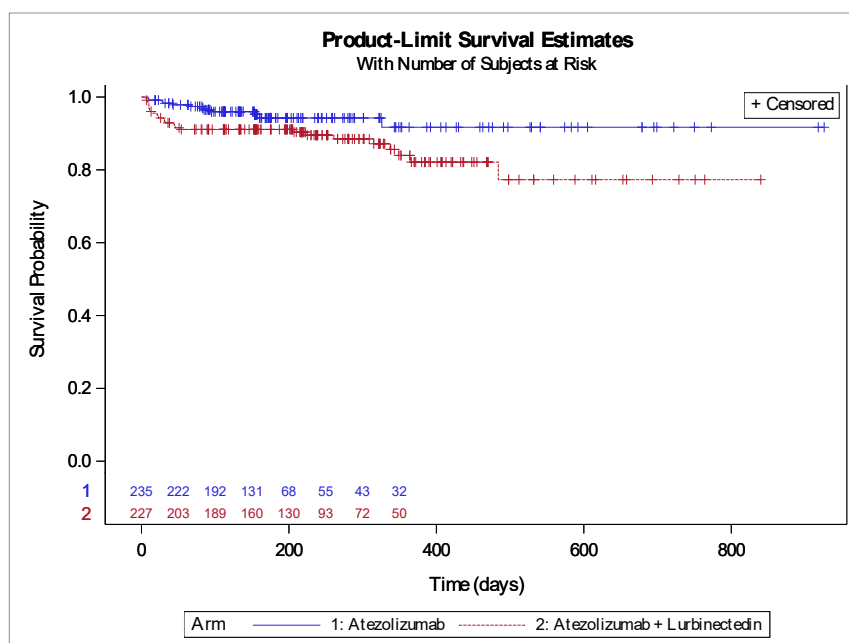


Abbildung 161: Kaplan-Meier plot for AE grade 4, patients with PR/SD to induction treatment, IMforte trial, Safety Analysis Set, CCOD 12 February 2025

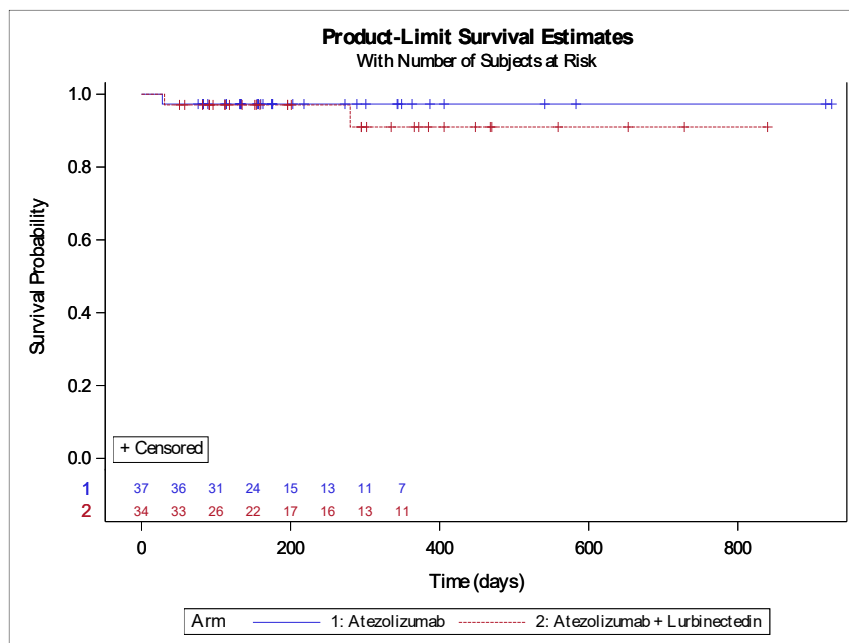


Abbildung 162: Kaplan-Meier plot for AE grade 5, patients receiving PCI prior to randomization, IMforte trial, Safety Analysis Set, CCOD 12 February 2025

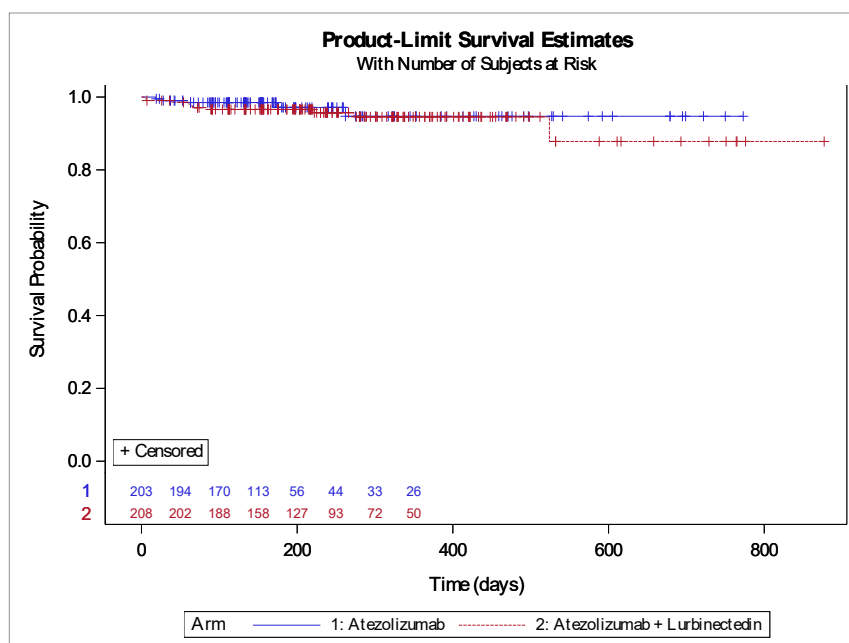


Abbildung 163: Kaplan-Meier plot for AE grade 5, patients not receiving PCI prior to randomization, IMforte trial, Safety Analysis Set, CCOD 12 February 2025

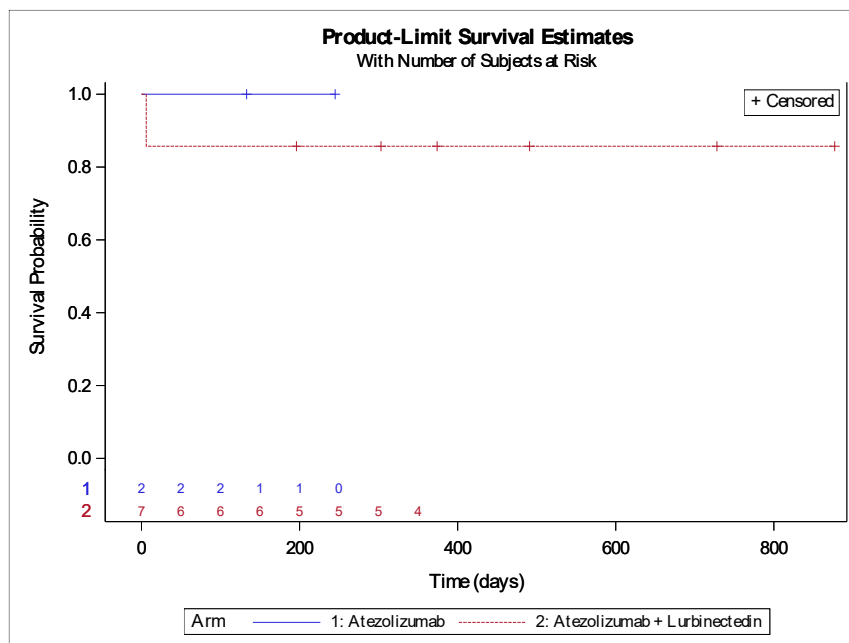


Abbildung 164: Kaplan-Meier plot for AE grade 5, patients with CR to induction treatment, IMforte trial, Safety Analysis Set, CCOD 12 February 2025

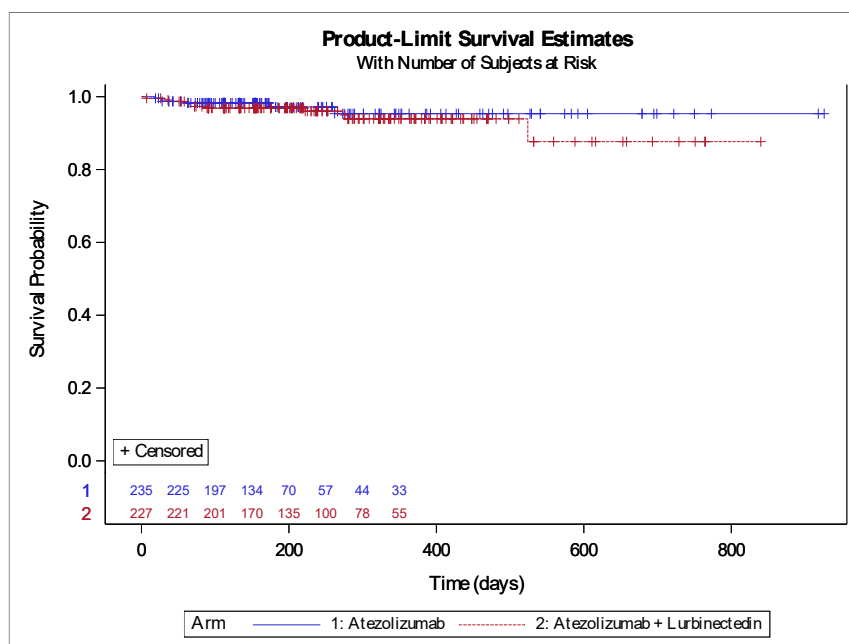


Abbildung 165: Kaplan-Meier plot for AE grade 5, patients with SD/PR to induction treatment, IMforte trial, Safety Analysis Set, CCOD 12 February 2025

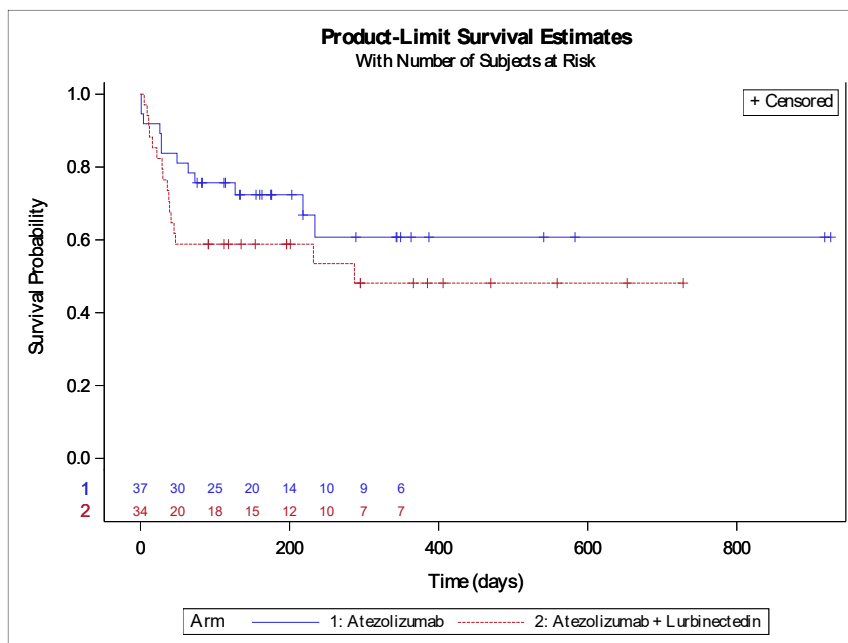


Abbildung 166: Kaplan-Meier plot for serious AE, patients receiving PCI prior to randomization, IMforte trial, Safety Analysis Set, CCOD 12 February 2025

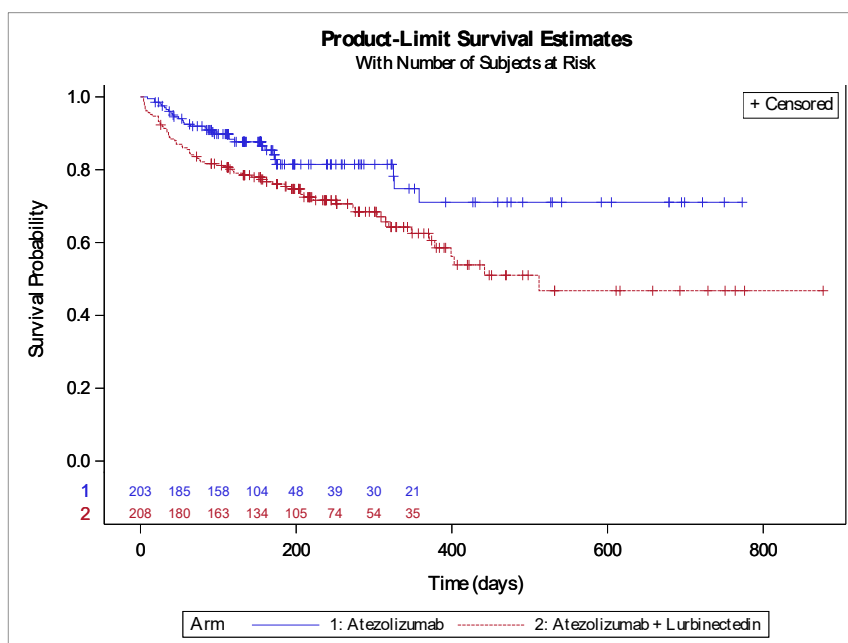


Abbildung 167: Kaplan-Meier plot for serious AE, patients not receiving PCI prior to randomization, IMforte trial, Safety Analysis Set, CCOD 12 February 2025

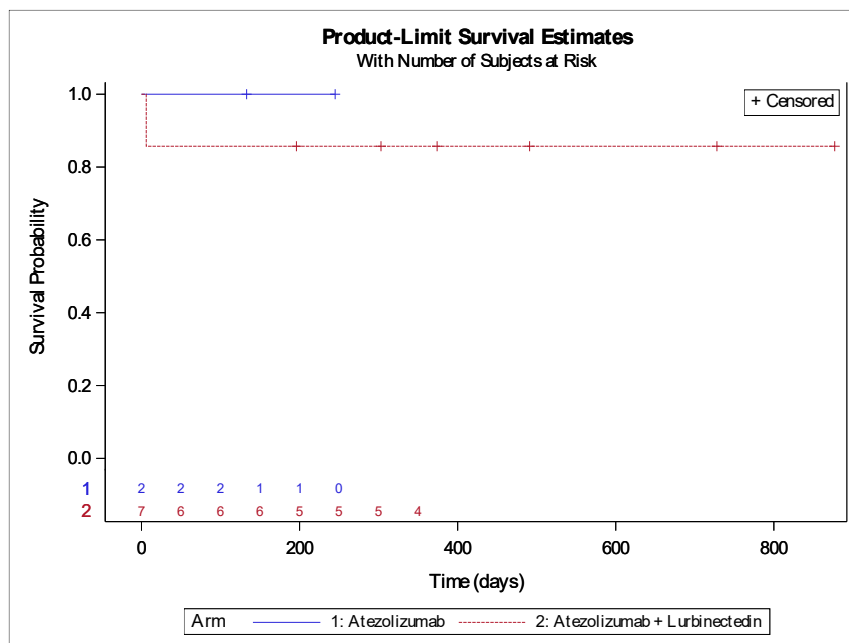


Abbildung 168: Kaplan-Meier plot for serious AE, patients with CR to induction treatment, IMfort trial, Safety Analysis Set, CCOD 12 February 2025

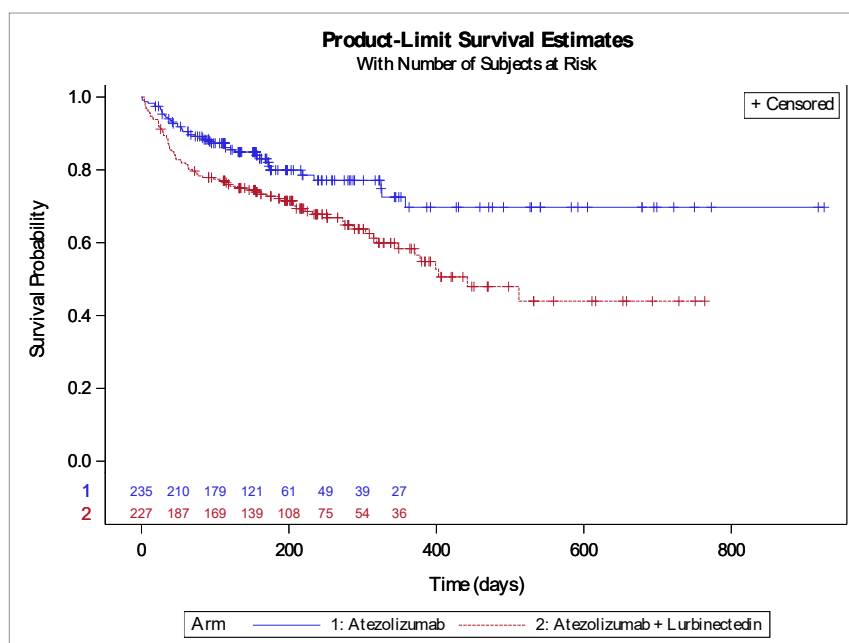


Abbildung 169: Kaplan-Meier plot for serious AE, patients with PR/SD to induction treatment, IMfort trial, Safety Analysis Set, CCOD 12 February 2025

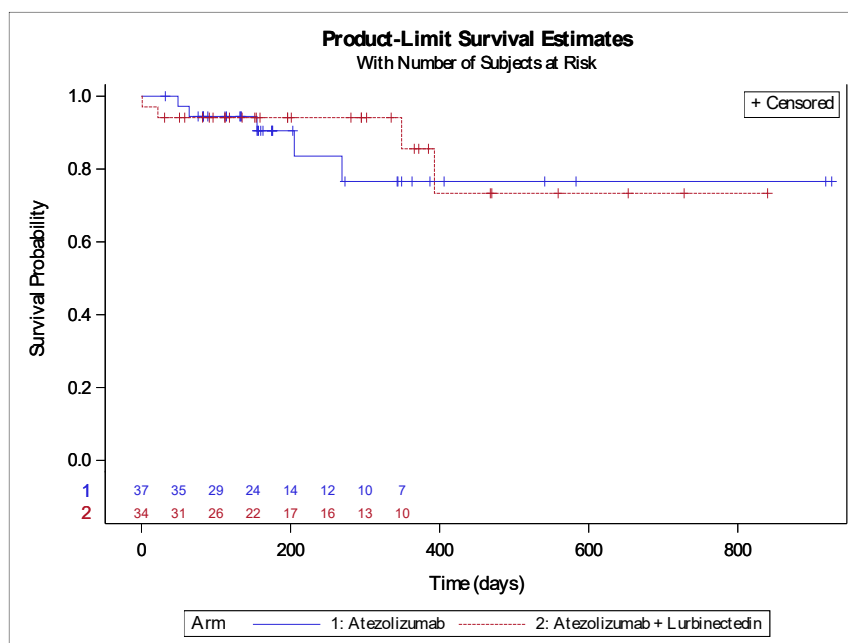


Abbildung 170: Kaplan-Meier plot for treatment discontinuation due to AE, patients receiving PCI prior to randomization, IMforte trial, Safety Analysis Set, CCOD 12 February 2025

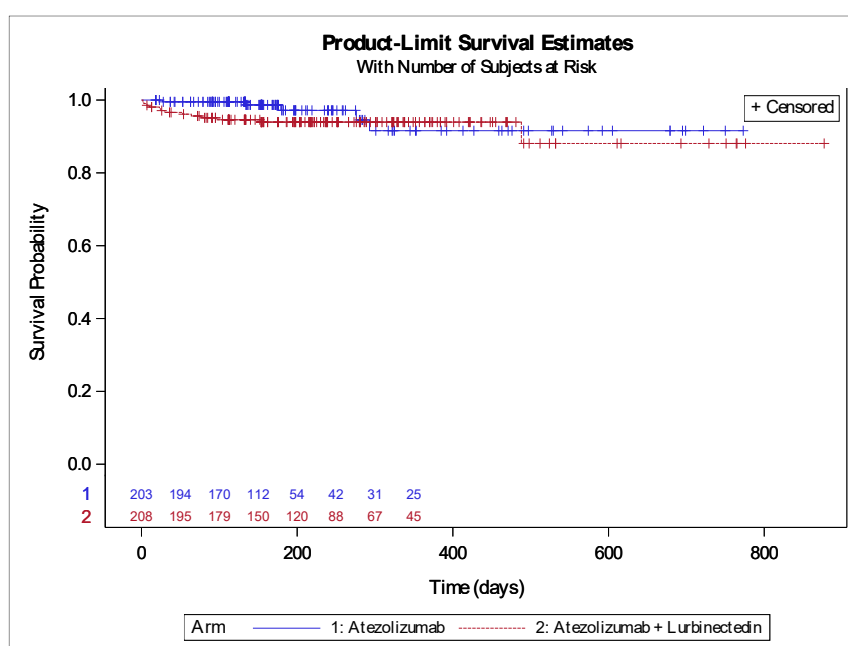


Abbildung 171: Kaplan-Meier plot for treatment discontinuation due to AE, patients not receiving PCI prior to randomization, IMforte trial, Safety Analysis Set, CCOD 12 February 2025

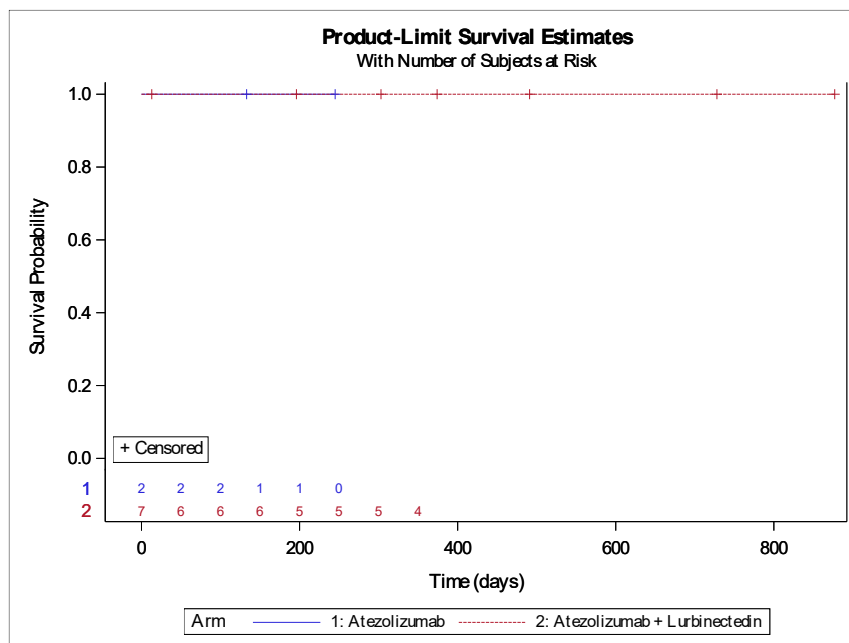


Abbildung 172: Kaplan-Meier plot for treatment discontinuation due to AE, patients with CR to induction treatment, IMforte trial, Safety Analysis Set, CCOD 12 February 2025

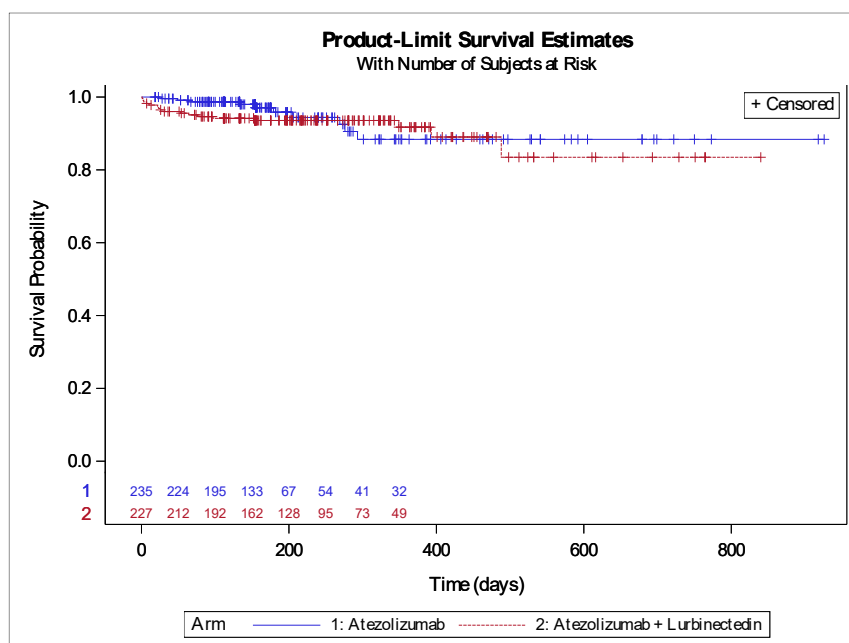


Abbildung 173: Kaplan-Meier plot for treatment discontinuation due to AE, patients with PR/SD to induction treatment, IMforte trial, Safety Analysis Set, CCOD 12 February 2025

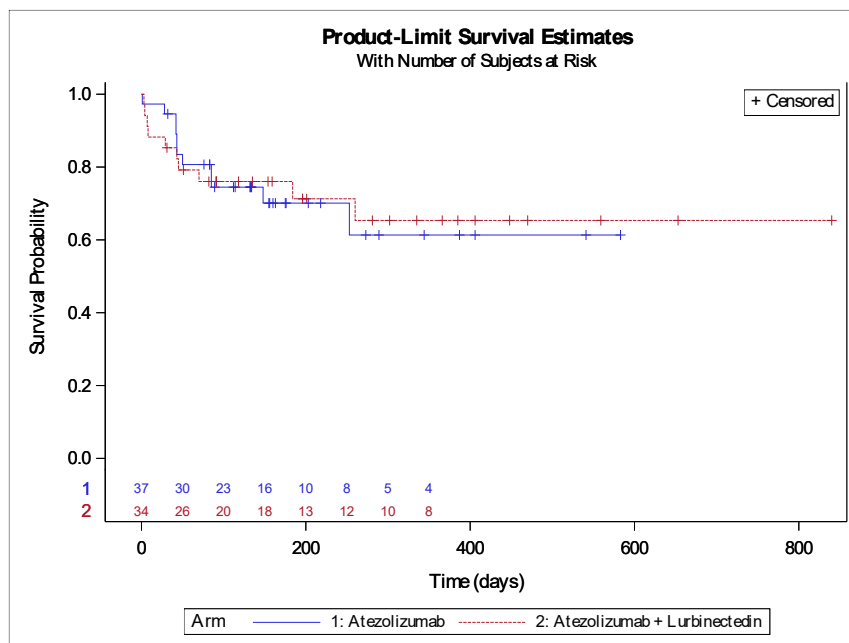


Abbildung 174: Kaplan-Meier plot for immune-related AE, patients receiving PCI prior to randomization, IMforte trial, Safety Analysis Set, CCOD 12 February 2025

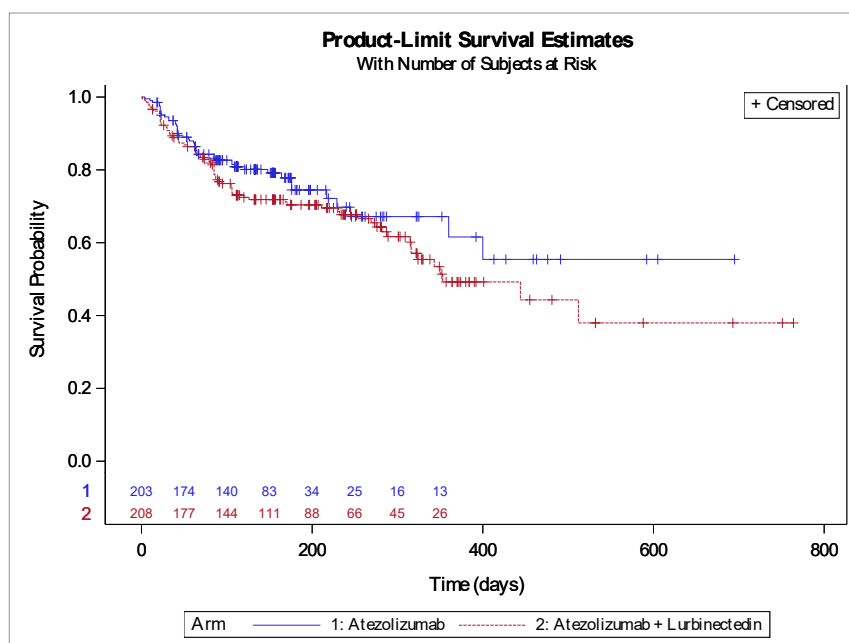


Abbildung 175: Kaplan-Meier plot for immune-related AE, patients not receiving PCI prior to randomization, IMforte trial, Safety Analysis Set, CCOD 12 February 2025

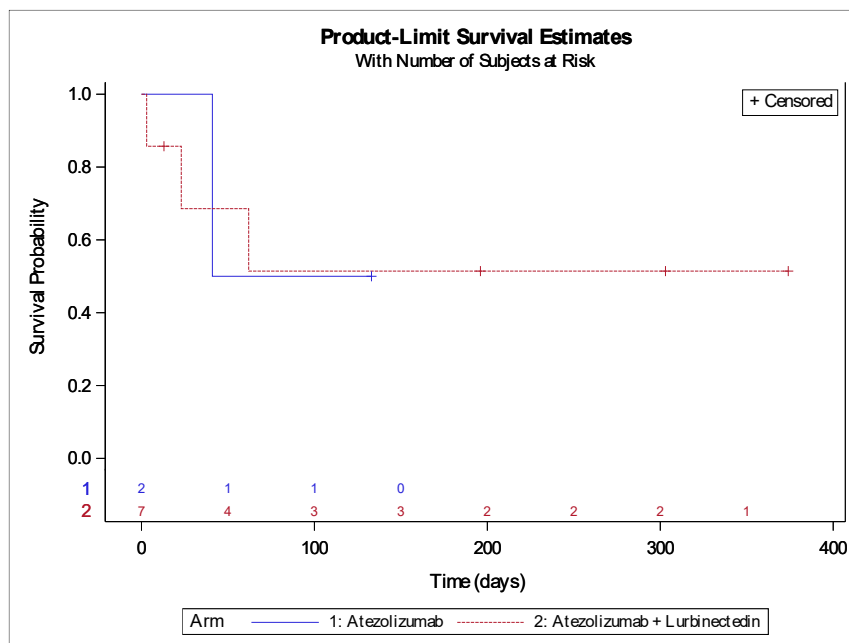


Abbildung 176: Kaplan-Meier plot for immune-related AE, patients with CR to induction treatment, IMforte trial, Safety Analysis Set, CCOD 12 February 2025

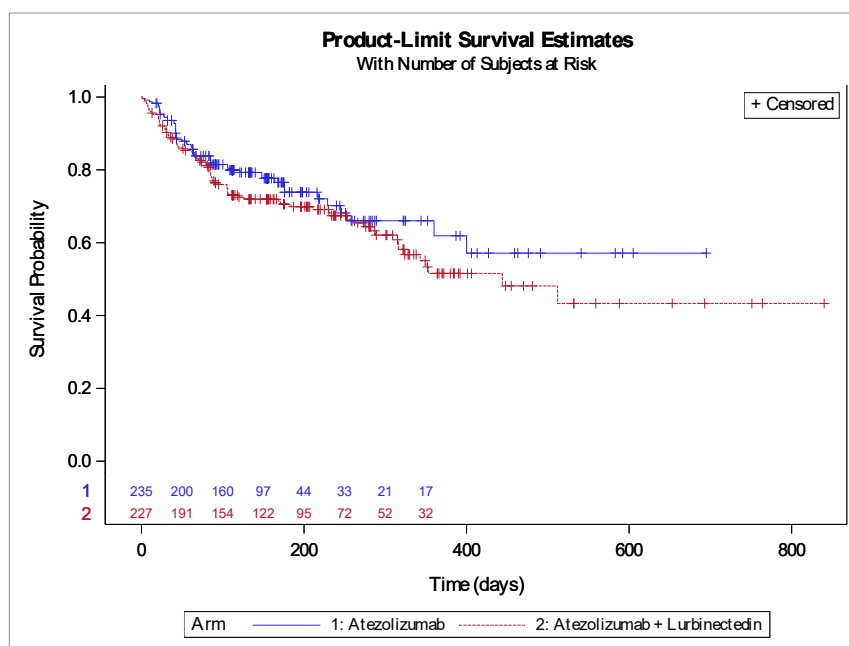


Abbildung 177: Kaplan-Meier plot for immune-related AE, patients with PR/SD to induction treatment, IMforte trial, Safety Analysis Set, CCOD 12 February 2025