**Supplementary materials**

**Methods: data collected and definitions**

*Biological parameters*

The list of baseline biological abnormalities collected before ICI initiation included complete blood count (CBC), thyroid-stimulating hormone (TSH), serum creatinine, liver enzymes and autoantibodies routinely measured at our institution: antinuclear antibodies, anti-thyroid antibodies and anti-CCP (cyclic citrullinated peptide) antibodies. Normal values were defined by the laboratory in charge. Abnormal CBC was considered if at least one of the following parameters had abnormal values: haemoglobin, lymphocytes, neutrophils, monocytes or platelet counts.

*Comorbidities*

Patients were considered an ex-smoker if they had stopped smoking at least 3 years before the first dose of anti-PD-(L)1.

*Immune related adverse events*

AEs were regarded as being almost confirmed irAEs if competing diagnoses were excluded by multidisciplinary consensus and if corticosteroid therapy led to a significant clinical improvement. AEs were considered if they had occurred after the first dose of PD-1 or PD-L1 inhibitor administration and were categorised by organ/system. One AE could involve several sites. Potential delayed AEs (after the last dose if treatment was stopped definitely) were also taken into account.

**Table S1. Prognostic factors for overall survival and progression-free survival in univariate and multivariate analyses.**

|  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Patient characteristics** | **N (%)** | **Overall survival** | | | | | **Progression free survival** | | | | | |
| **Median**  **(IQR: 25-75th)** | **Univariate analysis** | | **Multivariate analysis\*** | | **Median**  **(IQR: 25-75th)** | **Univariate analysis** | | | **Multivariate analysis\*** | |
| **Hazard Ratio [95% CI]** | ***p*** | **Hazard Ratio [95% CI]** | ***p*** | **Hazard Ratio [95% CI]** | | ***p*** | **Hazard Ratio [95% CI]** | ***p*** |
| **Age** | | | |  |  |  |  |  | |  |  |  |
| **<70 years** | 127 (63) | 8.1 (3.9-25.4) | Ref | 0.1176 | NI | NI | 4.1 (1.4-14.5) | Ref | | 0.0859 | Ref | 0.3614 |
| **≥70 years** | 74 (37) | 14.9 (4.0-NR) | 0.72 [0.48-1.09] |  |  |  | 5.8 (1.8-NR) | 0.72 [0.50-1.05] | |  | 0.81 [0.51-1.28] |  |
| **Smoking status (md=4)** | | | |  |  |  |  |  | |  |  |  |
| **Never** | 25 (13) | 30 (8-49) | Ref | Ref | Ref | Ref | 11.8 (3.4-44.2) | Ref | | Ref | NI | NI |
| **Current smoker** | 110 (56) | 8 (4-20) | 1.99 [0.98-4.03] | 0.0555 | 0.85 [0.33-2.15] | 0.7281 | 3.7 (1.3-17.4) | 1.47 [0.83-2.61] | | 0.1911 |  |  |
| **Ex-smoker** | 62 (32) | 12 (4-27) | 1.65 [0.78-3.48] | 0.1881 | 0.87 [0.33-2.29] | 0.7806 | 5.0 (2.0-21.5) | 1.19 [0.64-2.21] | | 0.5752 |  |  |
| **Pre-existing autoimmune conditions (md=4)** | | | |  |  |  |  |  | |  |  |  |
| **No** | 172 (87) | 9.5 (3.9-29.6) | Ref | 0.6304 | NI | NI | 4.3 (1.4-17.4) | Ref | | 0.2805 | NI | NI |
| **Yes** | 25 (13) | 10.7 (5.5-NR) | 0.86 [0.47-1.58] |  |  |  | 6.1 (1.9-NR) | 0.73 [0.41-1.29] | |  |  |  |
| **Corticosteroids at ICI initiation (md=12)** | | | |  |  |  |  |  | |  |  |  |
| **No** | 129 (68) | 10.4 (4.0-29.6) | Ref | Ref | NI | NI | 4.6 (1.5-21.5) | Ref | | Ref | NI | NI |
| **Inhaled/topical** | 11 (6) | 21.3 (16.7-NR) | 0.77 [0.28-2.12] | 0.6142 |  |  | 7.0 (2.1-NR) | 0.98 [0.43-2.25] | | 0.9672 |  |  |
| **Oral/Injectable** | 49 (26) | 6.5 (3.6-15.8) | 1.43 [0.92-2.24] | 0.1137 |  |  | 4.2 (1.1-14.5) | 1.16 [0.77-1.76] | | 0.4780 |  |  |
| **PPIs at ICI initiation (md=16)** | | | |  |  |  |  |  | |  |  |  |
| **No** | 104 (56) | 15.8 (5.0-35.3) | Ref | **0.0044** | Ref | 0.2551 | 5.3 (1.6-44.2) | Ref | | **0.0156** | Ref | 0.8356 |
| **Yes** | 81 (44) | 6.5 (2.5-15.4) | 1.78 [1.20-2.65] |  | 1.30 [0.83-2.04] |  | 4.1 (0.7-10.6) | 1.57 [1.09-2.25] | |  | 0.96 [0.64-1.44] |  |
| **Antibiotics in the last 30 days or at ICI initiation (md=13)** | | |  |  |  |  |  |  | |  |  |  |
| **No** | 139 (74) | 11.1 (4.8-35.3) | Ref | **<0.0001** | Ref | 0.1578 | 5.5 (1.6-32.3) | Ref | | **0.0005** | Ref | 0.3346 |
| **Yes** | 49 (26) | 4.3 (1.3-10.7) | 2.33 [1.55-3.52] |  | 1.43 [0.87-2.34] |  | 2.3 (0.7-5.5) | 2.00 [1.36-2.96] | |  | 1.25 [0.79-1.97] |  |
| **Complete blood count (md=13)** | | |  |  |  |  |  | |  |  |  |  |
| **Normal** | 49 (26) | 26.6 (7.5-49.0) | Ref | **<0.0001** | Ref | **0.0103** | 21.5 (3.3-44.2) | Ref | | **0.0012** | Ref | **0.0024** |
| **Abnormal** | 139 (74) | 6.7 (2.5-20.1) | 3.20 [1.79-5.73] |  | 2.48 [1.24-4.96] |  | 3.6 (0.9-13.3) | 2.12 [1.35-3.34] | |  | 2.38 [1.36-4.17] |  |
| **TSH (md=52)** | | | |  |  |  |  |  | |  |  |  |
| **Normal** | 126 (85) | 11.1 (3.9-26.6) | Ref | Ref | NI | NI | 5.0 (1.5-21.5) | Ref | | Ref | NI | NI |
| **Low** | 14 (9) | 5.3 (4.0-20.8) | 1.47 [0.75-2.86] | 0.2619 |  |  | 1.9 (0.4-5.5) | 1.47 [0.78-2.77] | | 0.2322 |  |  |
| **High** | 9 (6) | 8.9 (5.6-10.6) | 1.37 [0.59-3.17] | 0.4620 |  |  | 4.3 (3.6-6.1) | 1.23 [0.57-2.67] | | 0.5990 |  |  |
| **Autoantibodies (md=70)** | | | |  |  |  |  |  | |  |  |  |
| **Absence** | 103 (79) | 10.6 (4.3-26.6) | Ref | 0.1462 | NI | NI | 1.5 (0.5-5.3) | Ref | | **0.0398\*\*** | NI | NI |
| **Presence** | 28 (21) | 5.6 (2.3-20.0) | 1.50 [0.87-2.61] |  |  |  | 5.5 (2.1-21.5) | 1.68 [1.03-2.75] | |  |  |  |
| **Liver enzymes (md=21)** | | |  |  |  |  |  |  | |  |  |  |
| **Normal** | 106 (59) | 11.1 (5.9-29.6) | Ref | **0.0011** | Ref | 0.1630 | 6.4 (2.0-44.2) | Ref | | **0.0020** | Ref | 0.2263 |
| **High** | 74 (41) | 5.4 (1.6-17.6) | 1.93 [1.30-2.86] |  | 1.39 [0.88-2.20] |  | 2.3 (0.5-12.9) | 1.78 [1.24-2.56] | |  | 1.30 [0.85-1.99] |  |
| **Serum creatinine (md=16)** | | |  |  |  |  |  |  | |  |  |  |
| **Normal** | 149 (81) | 7.5 (3.7-25.4) | Ref | 0.3689 | NI | NI | 4.1 (1.4-17.2) | Ref | | 0.2994 | NI | NI |
| **High** | 36 (19) | 14.5 (4.3-29.6) | 0.80 [0.49-1.31] |  |  |  | 6.4 (2.1-NR) | 0.79 [0.50-1.24] | |  |  |  |
| **Transient interruption** | | |  |  |  |  |  |  | |  |  |  |
| **No** | 83 (41) | 3.9 (1.2-7.2) | Ref | **<0.0001** | Ref | **<0.0001** | 1.4 (0.5-2.4) | Ref | | **<0.0001** | Ref | **<0.0001** |
| **Yes** | 118 (59) | 20.0 (7.4-49.0) | 0.18 [0.12-0.28] |  | 0.18 [0.11-0.30] |  | 12.9 (4.6-44.2) | 0.14 [0.09-0.21] | |  | 0.13 [0.08-0.20] |  |
| **Adverse event** | | |  |  |  |  |  |  | |  |  |  |
| **No** | 36 (18) | 3.8 (1.6-9.5) | Ref | **0.0002** | Ref | **0.0083** | 1.6 (0.2-4.2) | Ref | | **<0.0001** | Ref | **0.0277** |
| **Yes** | 165 (82) | 11.1 (4.8-29.9) | 0.41 [0.26-0.66] |  | 0.45 [0.25-0.82] |  | 5.5 (1.6-32.3) | 0.43 [0.28-0.66] | |  | 0.54 [0.31-0.93] |  |
| **Internal medicine consultation before ICI initiation** | | | |  |  |  |  |  | |  |  |  |
| **No** | 72 (36) | 12.2 (5.4-49.0) | Ref | 0.0516 | Ref | 0.4598 | 4.8 (1.6-44.2) | Ref | | 0.2426 | NI | NI |
| **Yes** | 129 (64) | 8.9 (3.7-20.8) | 1.52 [0.99-2.31] |  | 1.26 [0.68-2.34] |  | 4.6 (1.4-17.2) | 1.24 [0.86-1.80] | |  |  |  |
| **Cancer type** | | | |  |  |  |  |  | |  |  |  |
| **NSCLC** | 147 (73) | 10.4 (4.0-25.4) | Ref | Ref | Ref | Ref | 5.0 (1.5-17.4) | Ref | | Ref | Ref | Ref |
| **SCLC** | 10 (5) | 3.7 (0.3-NR) | 2.51 [0.99-6.32] | 0.0511 | 3.60 [1.35-9.57] | **0.0103** | 1.6 (0-5.3) | 1.97 [0.95-4.09] | | 0.0674 | 2.34 [1.07-5.12] | **0.0326** |
| **CHL** | 3 (<1) | NR | 0.54 [0.08-3.91] | 0.5443 | 0.47 [0.06-3.89] | 0.4836 | 10.8 (4.1-17.4) | 0.80 [0.20-3.26] | | 0.7597 | 0.35 [0.05-2.67] | 0.3097 |
| **RCC** | 12 (6) | 29.9 (6.8-NR) | 0.36 [0.13-0.98] | **0.0456** | 0.29 [0.07-1.18] | 0.0841 | NR | 0.44 [0.18-1.08] | | 0.0724 | 0.51 [0.18-1.45] | 0.2082 |
| **HNSCC** | 9 (4) | 8.3 (3.6-10.8) | 1.15 [0.42-3.15] | 0.7851 | 5.38 [1.21-23.90] | **0.0271** | 4.0 (3.0-5.0) | 1.31 [0.57-2.99] | | 0.5250 | 2.12 [0.65-6.91] | 0.2138 |
| **TCC** | 20 (10) | 7.2 (1.3-NR) | 1.27 [0.65-2.45] | 0.4829 | 1.02 [0.30-3.47] | 0.9738 | 2.1 (0-NR) | 1.24 [0.69-2.22] | | 0.4691 | 0.70 [0.27-1.79] | 0.4516 |

\*Multivariate analysis was performed only for parameters with p≤0.10 in univariate analysis.

\*\*Not included because too much data is missing.

CHL: Classical Hodgkin’s lymphoma; CI: confidence interval; HNSCC: head and neck squamous cell carcinoma; ICI: immune checkpoint inhibitor; IQR: interquartile range; MD: missing data; NI: not Included; NR: not reached; NSCLC: non-small cell lung cancer; PPIs: proton pump inhibitors; Ref: reference; RCC: renal cell carcinoma; SCLC: small cell lung cancer; TCC: transitional cell carcinoma; TSH: thyroid-stimulating hormone.

**Table S2. Treatment interruptions and their reasons.**

|  |  |
| --- | --- |
| **Treatment interruption** | **All patients**  **(n=201)** |
| **Transient ICI interruptions**  **Total** | 338 |
| **Reasons for interruption, n (%)**  **Delay due to medical check-up**  **Potential irAE**  **Health condition unrelated to ICI**  **Patient’s choice**  **Disease remission**  **Not specified** | 130 (38)  65 (19)  26 (8)  10 (3)  4 (1)  103 (30) |
| **Patients with ICI interruptions, n (%)**  **Yes** | 118 (59% of 201) |
| **Duration of interruption, days**  **Median (IQR: 25-75th)** | 35 (27-50) |
| **Patients with ICI final stop, n (%)**  **Yes** | 164 (82) |
| **Reason for final stop\***  **Disease progression**  **Potential irAE**  **Health condition unrelated to ICI**  **Disease remission**  **Death**  **Patient’s choice**  **End of recommended duration**  **Mutation detection: strategy shift**  **NSCLC transformation into SCLC**  **No clear response to treatment**  **Stable disease** | (n=203)\*  84 (41)  26 (13)  23 (11)  22 (11)  15 (7)  10 (5)  4 (2)  2 (1)  2 (1)  1 (<1)  1 (<1) |
| **Not specified** | 13 (6) |

\*One final stop could have several reasons.

ICI: immune checkpoint inhibitor; irAE: immune-related adverse event; NS: not significant; NSCLC: non-small cell lung cancer; PD-1: programmed cell death-1; PD-L1: programmed cell death-ligand 1; SCLC: small cell lung cancer.

**Table S3. Patient characteristics depending on AE severity and probability of being an irAE (univariate analysis).**

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Patient characteristics** | **Primary endpoint:**  **Patients with at least “likely” irAE and grade >2** | | | **Secondary endpoint:**  **Patients with at least “likely” irAE and grade >3** | | | **Alternative secondary endpoint:**  **Patients with at least “very likely” irAE and grade >2** | | |
|  | **Yes**  **(n=110)** | **No**  **(n=91)** | ***p*** | **Yes**  **(n=71)** | **No**  **(n=130)** | ***p*** | **Yes**  **(n=61)** | **No**  **(n=140)** | ***p*** |
| **Age, n (%)** |  |  | 0.8838 |  |  | 0.7923 |  |  | 0.8630 |
| **<70 years** | 70 (64) | 57 (63) |  | 44 (62) | 83 (64) |  | 38 (62) | 89 (64) |  |
| **≥70 years** | 40 (36) | 34 (37) |  | 27 (38) | 47 (36) |  | 23 (38) | 51 (36) |  |
| **Smoking status, n (%)** | (n=107) | (n=90) | 0.7344 | (n=69) | (n=128) | 0.9440 | (n=60) | (n=137) | 0.2430 |
| **Never** | 12 (11) | 13 (14) |  | 8 (12) | 17 (13) |  | 4 (7) | 21 (15) |  |
| **Current smoker** | 62 (58) | 48 (53) |  | 39 (57) | 71 (55) |  | 36 (60) | 74 (54) |  |
| **Ex-smoker** | 33 (31) | 29 (32) |  | 22 (32) | 40 (32) |  | 20 (33) | 42 (31) |  |
| **Prior autoimmune conditions, (%)** |  | (n=87) | 0.6538 |  | (n=126) | 0.1826 |  | (n=136) | 0.2957 |
| **No** | 95 (86) | 77 (89) |  | 59 (83) | 113 (90) |  | 51 (84) | 121 (89) |  |
| **Yes** | 15 (14) | 10 (11) |  | 12 (17) | 13 (10) |  | 10 (16) | 15 (11) |  |
| **Corticosteroids at ICI initiation, n (%)** | (n=104) | (n=85) | 0.4412 | (n=67) | (n=122) | 0.8235 | (n=58) | (n=131) | 0.0934 |
| **No** | 75 (72) | 54 (64) |  | 47 (70) | 82 (67) |  | 46 (79) | 83 (63) |  |
| **Inhaled/topical** | 5 (5) | 6 (7) |  | 3 (5) | 8 (7) |  | 2 (3) | 9 (7) |  |
| **Oral/injectable** | 24 (23) | 25 (29) |  | 17 (25) | 32 (26%) |  | 10 (17) | 39 (30) |  |
| **PPIs at ICI initiation, n (%)** | (n=100) | (n=85) | 0.8157 | (n=65) | (n=120) | 0.8866 | (n=56) | (n=129) | 0.4165 |
| **No** | 57 (57) | 47 (55) |  | 37 (57) | 67 (56) |  | 34 (61) | 70 (54) |  |
| **Yes** | 43 (43) | 38 (45) |  | 28 (43) | 53 (44) |  | 22 (39) | 59 (46) |  |
| **Antibiotics, 0-30 days before ICI, n (%)** | (n=102) | (n=86) | 0.4206 | (n=66) | (n=122) | 0.3301 | (n=57) | (n=131) | 0.7569 |
| **No** | 73 (72) | 66 (77) |  | 46 (70) | 93 (76) |  | 43 (75) | 96 (73) |  |
| **Yes** | 29 (28) | 20 (23) |  | 20 (30) | 29 (24) |  | 14 (25) | 35 (27) |  |
| **Complete blood count** | (n=104) | (n=84) | 0.7116 | (n=67) | (n=121) | 0.1216 | (n=58) | (n=130) | 0.7508 |
| **Normal** | 26 (25) | 23 (27) |  | 13 (19) | 36 (30) |  | 16 (28) | 33 (25) |  |
| **Abnormal** | 78 (75) | 61 (73) |  | 54 (81) | 85 (70) |  | 42 (72) | 97 (75) |  |
| **TSH, n (%)** | (n=82) | (n=67) | 0.1718 | (n=53) | (n=96) | **0.0225** | (n=46) | (n=103) | 0.5094 |
| **Low** | 9 (11) | 5 (7) |  | 8 (15) | 6 (6) |  | 5 (11) | 9 (9) |  |
| **Normal** | 70 (85) | 56 (84) |  | 44 (83) | 82 (85) |  | 39 (85) | 87 (84) |  |
| **High** | 3 (4) | 6 (9) |  | 1 (2) | 8 (8) |  | 2 (4) | 7 (7) |  |
| **Autoantibodies, n (%)** | (n=74) | (n=57) | 0.6110 | (n=47) | (n=84) | **0.0277** | (n=42) | (n=89) | 0.6404 |
| **Absence** | 57 (77) | 46 (81) |  | 32 (68) | 71 (85) |  | 32 (76) | 18 (20) |  |
| **Presence** | 17 (23) | 11 (19) |  | 15 (32) | 13 (15) |  | 10 (24) | 71 (80) |  |
| **Liver enzymes, n (%)** | (n=102) | (n=78) | 0.0697 | (n=67) | (n=113) | 0.6284 | (n=55) | (n=125) | 0.1294 |
| **Normal** | 66 (65) | 40 (51) |  | 41 (61) | 65 (58) |  | 37 (67) | 69 (55) |  |
| **High** | 36 (35) | 38 (49) |  | 26 (39) | 48 (42) |  | 18 (33) | 56 (45) |  |
| **Serum creatinine, n (%)** | (n=102) | (n=83) | 0.1211 | (n=68) | (n=117) | **0.0263** | (n=55) | (n=130) | 0.1803 |
| **Normal**  **High** | 78 (76)  24 (24) | 71 (86)  12 (14) |  | 49 (72)  19 (28) | 100 (85)  17 (15) |  | 41 (75)  14 (25) | 108 (83)  22 (17) |  |
| **Metastasis** |  |  | 0.6960 |  |  | 0.4275 |  |  | 0.6866 |
| **No** | 28 (25%) | 21 (23%) |  | 15 (21%) | 34 (26%) |  | 16 (26%) | 33 (24%) |  |
| **Yes** | 82 (75%) | 70 (77%) |  | 56 (79%) | 96 (74%) |  | 45 (74%) | 107 (76%) |  |
| **Line of treatment** |  |  | 0.3575 |  |  | 0.4089 |  |  | 0.6035 |
| **1** | 32 (29%) | 32 (35%) |  | 20 (28%) | 44 (34%) |  | 21 (34%) | 43 (31%) |  |
| **≥2** | 78 (71%) | 59 (65%) |  | 51 (72%) | 86 (66%) |  | 40 (66%) | 97 (69%) |  |
| **Combination with chemotherapy** |  |  | 1.0000 |  |  | 1.0000 |  |  | 0.7805 |
| **Yes** | 9 (8%) | 7 (8%) |  | 6 (8%) | 10 (8%) |  | 4 (7%) | 12 (9%) |  |
| **No** | 101 (92%) | 84 (92%) |  | 65 (92%) | 120 (92%) |  | 57 (93%) | 128 (91%) |  |

AE: adverse event; ICI: immune checkpoint inhibitor; irAE: immune-related adverse event; PPI: proton pump inhibitor; TSH: thyroid-stimulating hormone.

**Table S4. Severe toxicities**

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **n**  **AE** | **n patient** | **ICI** | **irAE probability\*** | **Grade\*\*** | **n**  **dose\*\*\*** | **Site** | **Description** |
| 1 | 1 | nivolumab | almost confirmed | 3 | 3 | systemic | PMR-like |
| 2 | 2 | nivolumab | very likely | 3 | 5 | gastrointestinal | colitis |
| 3 | 2 | nivolumab | almost confirmed | 3 | 24 | liver | hepatitis |
| 4 | 3 | nivolumab | very likely | 3 | 16 | endocrine | diabetes |
| 5 | 4 | nivolumab | very likely | 3 | 1 | endocrine | hypercalcemia |
| 6 | 5 | nivolumab | very likely | 3 | 20 | liver | hepatitis |
| 7 | 6 | nivolumab | almost confirmed | 3 | 2 | cutaneous | psoriasis |
| 8 | 7 | nivolumab | very likely | 3 | 1 | systemic | SIRS |
| 9 | 8 | nivolumab | very likely | 3 | 1 | endocrine | hyponatremia |
| 10 | 9 | nivolumab | almost confirmed | 3 | 6 | endocrine | hypothyroidism |
| 11 | 10 | nivolumab | very likely | 3 | 1 | systemic | PMR-like |
| 12 | 11 | nivolumab | almost confirmed | 3 | 3 | endocrine | hyperthyroidism |
| 13 | 12 | nivolumab | very likely | 3 | 1 | liver | hepatitis |
| 14 | 13 | nivolumab | almost confirmed | 3 | 1 | cutaneous | psoriasis (worsening) |
| 15 | 14 | nivolumab | almost confirmed | 3 | 3 | systemic | PMR-like |
| 16 | 15 | nivolumab | very likely | 3 | 1 | systemic | SIRS |
| 17 | 16 | nivolumab | very likely | 3 | 5 | respiratory | ILD |
| 18 | 17 | nivolumab | almost confirmed | 3 | 9 | endocrine | hyperthyroidism |
| 19 | 18 | nivolumab | very likely | 3 | 5 | gastrointestinal | colitis |
| 20 | 18 | nivolumab | very likely | 3 | 8 | liver | hepatitis |
| 21 | 19 | nivolumab | very likely | 4 | 22 | liver | hepatitis |
| 22 | 20 | pembrolizumab | almost confirmed | 4 | 2 | cutaneous | psoriasis |
| 23 | 21 | pembrolizumab | almost confirmed | 4 | 1 | cardiac | myocarditis |
| 24 | 22 | pembrolizumab | almost confirmed | 3 | 1 | respiratory | ILD |
| 25 | 23 | pembrolizumab | very likely | 3 | 3 | respiratory | ILD |
| 26 | 24 | pembrolizumab | almost confirmed | 3 | 10 | endocrine | adrenal insufficiency |
| 27 | 25 | pembrolizumab | very likely | 4 | 1 | respiratory | pleurisy |
| 28 | 26 | pembrolizumab | very likely | 3 | 1 | respiratory | ILD |
| 29 | 27 | pembrolizumab | very likely | 3 | 4 | endocrine | hypothyroidism |
| 30 | 28 | durvalumab | almost confirmed | 3 | 3 | endocrine | hyperthyroidism |
| 31 | 28 | durvalumab | almost confirmed | 3 | 13 | liver | hepatitis |
| 32 | 29 | durvalumab | almost confirmed | 3 | 3 | endocrine | hyperthyroidism |
| 33 | 30 | durvalumab | almost confirmed | 3 | 1 | systemic | PMR (relapse) |
| 34 | 31 | atezolizumab | very likely | 3 | 2 | liver | hepatitis |
| 35 | 32 | atezolizumab | very likely | 3 | 7 | liver + cutaneous | dermatitis + hepatitis |
| 36 | 33 | atezolizumab | very likely | 3 | 13 | cutaneous | mucositis |

\*A probability scale of being an irAE was used (unlikely, likely, very likely, almost confirmed).

\*\*Toxicity was evaluated by study investigators according to Common Terminology Criteria for Adverse Events

(CTCAE version 5.0) [12,13].

\*\*\*Number of cures administered before the irAE occurrence.

AE: adverse event; ICI: immune checkpoint inhibitor; ILD: interstitial lung disease; irAE: immune-related adverse event; PMR: polymyalgia rheumatica; SIRS: systemic inflammatory response syndrome.