**Supplementary Table 1:** Reasons for Pembrolizumab Treatment discontinuation

|  |  |  |  |
| --- | --- | --- | --- |
| **Reason** |  |  | **Overall Patients**  **n (%)** |
| Progressive disease or clinical progressive disease | | | 474 (53.9) |
| Unacceptable toxicity |  |  | 55 (6.3) |
| Lost to follow up |  |  | 39 (4.4) |
| Patient’s decision |  |  | 4 (0.5) |
| Clinical decision |  |  | 46 (5.2) |
| Death |  |  | 120 (13.6) |
| Not specified |  |  | 1 (0.1) |
| Therapy is still ongoing at the cutoff data |  |  | 141 (16.0) |

**Supplementary Table 2:** Response Rate

|  |  |
| --- | --- |
| **Best overall response** | **Overall patients**  **n (%)** |
| Complete response | 24 (2.7) |
| Partial response | 155 (17.6) |
| Stable disease | 204 (23.2) |
| Progressive disease | 228 (25.9) |
| Not yet documented | 269 (30.6) |

**Supplementary Table 3**: Adverse reaction management

| **Action taken** | **Overall patients**  **n (%)** |
| --- | --- |
| Suspension of one or more drug | 71 (8.07) |
|  |  |
| Permanent discontinuation of the treatment | 47 (5.3) |
|  |  |
| Dose reduction of one or more drugs | 0 (0.0) |
|  |  |
| Specific pharmacologic treatment for toxicity management | 177 (20.1) |
|  |  |
| Hospitalization or prolongation of hospitalization | 55 (6.25) |

**Supplementary Table 4**: univariables and multivariable model for Rw-PFS

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Variables** | **Univariable models** | | | **Multivariable model** | | |
| **Hazard Ratio** | **p-value** | **95% CI** | **Hazard Ratio** | **p-value** | **95% CI** |
| Smoker/Former smoker vs no smoker | 0.72 | 0.007 | 0.57-0.92 | 0.81 | 0.144 | 0.61-1.07 |
| PDL1 70-89% vs PDL1 50-69% | 0.90 | 0.368 | 0.73-1.11 | 0.82 | 0.125 | 0.64-1.05 |
| PDL1 ≥90% vs PDL1 50-69% | 0.64 | 0.001 | 0.49-0.83 | 0.62 | 0.001 | 0.46-0.83 |
| PS ECOG 1 vs PS ECOG 0 | 1.36 | <0.001 | 1.15-1.60 | 1.51 | <0.001 | 1.20-1.89 |
| PS ECOG 2 vs PS ECOG 0 | 2.56 | <0.001 | 1.94-3.38 | 2.36 | <0.001 | 1.50-3.69 |

**Supplementary Table 5**: univariables and multivariable model for Rw-OS

| **Variable by subgroup of therapy** | **Univariable models** | | | **Multivariable model** | | |
| --- | --- | --- | --- | --- | --- | --- |
| **HR** | **p-value** | **95% CI** | **HR** | **p-value** | **95% CI** |
| Age ≥75 years vs age <75 | 1.36 | 0.002 | 1.12-1.67 | 1.27 | 0.063 | 0.99-1.64 |
| Female vs Male | 0.77 | 0.015 | 0.62-0.95 | 0.83 | 0.188 | 0.64-1.09 |
| No squamo vs squamo (main effect) | 0.75 | 0.011 | 0.60-0.94 | 1.10 | 0.709 | 0.66-1.84 |
| No squamo vs squamo (time dependent effect) | - | - | - | 0.79 | 0.051 | 0.64-1.01 |
| PS ECOG 1 vs PS ECOG 0 (main effect) | 1.43 | <0.001 | 1.18-1.74 | 3.09 | <0.001 | 1.86-5.16 |
| PS ECOG 2 vs PS ECOG 0 (main effect) | 2.49 | <0.001 | 1.82-3.40 | 5.89 | <0.001 | 3.11-11.1 |
| PS ECOG 1 vs PS ECOG 0 (time dependent effect) | - | - | - | 0.67 | <0.001 | 0.54-0.84 |
| PS ECOG 2 vs PS ECOG 0 (time dependent effect) | - | - | - | 0.53 | <0.001 | 0.39-0.72 |
| Smoker+ex smoker vs no smoker | 1.37 | 0.045 | 1.01-1.87 | 1.32 | 0.077 | 0.97-1.82 |
|  |  |  |  |  |  |  |

**Supplementary Figure 1:** Kaplan – Meier curves for Rw-PFS in subgroup of interest. A) PD-L1 levels (50-69%; 70-89%; ≥ 90%) B) ECOG PS C) smoking status



C

B

A

**Supplementary Figure 2:** Kaplan – Meier curves of real world OS in subgroup of interest. A) age (<75 years vs ≥ 75 years) . B) Gender C) histological type D) smoking status E) ECOG PS



D

E

C

B

A