**SUPPLEMENTARY MATERIALS**

**Table S1. Additional baseline characteristics**

|  |  |  |
| --- | --- | --- |
| **Characteristics** | **Clinical Trial DataN = 241** | **Real-World Data (Flatiron)aN = 816** |
| BRAFV600 mutation status |  |  |
| BRAFV600E positive | -- | 199 (24.4) |
| BRAFV600K positive | -- | 39 (4.8) |
| BRAFV600E negative | -- | 1 (0.1) |
| Missing | -- | 577 (70.7) |
| M stage at treatment initiation, N (%) |  |  |
| Stage III | 6 (2.5) | -- |
| M0 | 5 (2.1) | -- |
| M1a | 0 (0) | -- |
| M1b | 0 (0) | -- |
| M1c | 1 (0.4) | -- |
| Stage IV | 235 (97.5) | -- |
| M0 | 0 (0) | -- |
| M1a | 37 (15.4) | -- |
| M1b | 48 (19.9) | -- |
| M1c | 150 (62.2) | -- |

**Table S2. Use of subsequent therapies in the CTD and RWD**

|  |  |  |
| --- | --- | --- |
| **Characteristics** | **Clinical Trial DataN = 241** | **Real-World Data (Flatiron)N = 816** |
| Any subsequent therapy, N (%) | 64 (26.6) | 378 (46.3) |
| Immunotherapy | 14 (21.9) | 274 (72.5) |
|  Pembrolizumab | 0 (0.0) | 159 (42.1) |
|  Nivolumab | 0 (0.0) | 132 (34.9) |
|  Ipilimumab | 1 (1.6) | 58 (15.3) |
|  Other immunotherapya | 13 (20.3) | 5 (1.3) |
| Other therapies | 50 (78.1) | 104 (27.5) |
|  Dabrafenib | 0 (0.0) | 76 (20.1) |
|  Trametinib | 0 (0.0) | 74 (19.6) |
|  Temozolomide | 14 (21.9) | 46 (12.2) |
|  Vemurafenib | 0 (0.0) | 37 (9.8) |
|  Paclitaxel | 11 (17.2) | 32 (8.5) |
|  Carboplatin | 14 (21.9) | 24 (6.3) |
|  Dacarbazine | 3 (4.7) | 16 (4.2) |
|  Cobimetinib | 0 (0.0) | 12 (3.2) |
|  Bevacizumab | 3 (4.7) | 9 (2.4) |
|  Fluorouracil | 0 (0.0) | 5 (1.3) |
|  Cisplatin | 9 (14.1) | 1 (0.3) |
|  Fotemustine | 9 (14.1) | 0 (0.0) |

Abbreviations: CTD, clinical trial data; RWD, real-world data

Note:

a Other immunotherapy included monotherapy or combination therapies including any of the following treatments: anti-CTLA4 antibody, durvalumab, interferon, interleukin, investigational immunotherapy, leukine, and T-VEC.

**Table S3. Multivariable Cox Proportional Hazards model for overall survival in the RWD**

|  |  |
| --- | --- |
| **Baseline Characteristics** | **Hazard Ratio (95% CI)**   |
| Age (years) | 1.01 (1.00, 1.02)\* |
| Male vs. female | 1.12 (0.92, 1.35) |
| White vs. other race | 0.99 (0.68, 1.45) |
| Race missing | 1.10 (0.64, 1.89) |
| Disease stage III vs. IV | 0.54 (0.41, 0.70)\* |
| Disease stage missing | 0.75 (0.61, 0.92)\* |
| ECOG performance status of 0 vs. 1 | 0.79 (0.60, 1.04) |
| ECOG performance status missing | 0.94 (0.74, 1.18) |
| BMI ≤ 25 vs. > 25 | 1.37 (1.13, 1.67)\* |
| BMI missing | 1.00 (0.70, 1.43) |
| LDH ≤ ULN vs. > ULN | 0.54 (0.44, 0.68)\* |
| LDH missing | 0.60 (0.48, 0.76)\* |
| Time from advanced diagnosis to ipilimumab initiation (months) | 1.00 (0.99, 1.01) |
| Received ≤ 1 prior systemic therapy | 0.85 (0.58, 1.25) |
| Received prior immunotherapy | 1.09 (0.78, 1.52) |

\*p-value < 0.05

Abbreviations: BMI, body mass index; CI, confidence interval; ECOG, Eastern Cooperative Oncology Group; LDH, lactate dehydrogenase; RWD, real-world data; ULN, upper limit of normal.