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| **Table S2. Detailed characteristics of the unfavorable subset of CUP patients** |
| **Characteristic** | **No. of patients (%)a** | ***P* valueb** |
| **Full-analysis set****(*n* = 130)** | **Biomarker-analysis set****(*n* = 72)** |
| Median age (range), years |  68 (37–95) | 68 (37–95) | 0.871 |
| Sex |  |  | 0.456 |
|  Male  |  73 (56) | 45 (63) |  |
|  Female |  57 (44) | 27 (38) |  |
| ECOG performance status |  |  | 0.942 |
|  0–1 |  80 (62) | 46 (64) |  |
|  2 |  25 (19) | 12 (17) |  |
|  3–4 |  13 (10) |  7 (10) |  |
|  Unknown (not recorded) | 12 (9) |  7 (10) |  |
| Smoking historyc |  |  | 0.621 |
|  Current or former |  72 (55) | 45 (63) |  |
|  Never |  39 (30) | 20 (28) |  |
|  Unknown (not recorded) |  19 (15) |  7 (10) |  |
| Metastatic lesions |  |  |  |
|  CNS |  8 (6) | 3 (4) | 0.750 |
|  Multiple lymph nodes only |  41 (32) | 24 (33) | 0.875 |
| Histology |  |  | 0.853 |
|  Squamous |  17 (13) |  9 (13) |  |
|  Adeno |  68 (52) | 39 (54) |  |
|  Undifferentiated |  35 (27) | 21 (29) |  |
|  Other |  10 (8)d |  3 (4)e |  |
| Serum albumin |  |  | 1.000 |
|  Normoalbuminemia (≥4.0 mg/dL) |  36 (28) | 20 (28) |  |
|  Hypoalbuminemia (<4.0 mg/dL) |  92 (71) | 52 (72) |  |
|  Not examined |  2 (2) |  |  |
| Serum LDH |  |  | 1.000 |
|  Not elevated (<223 IU/L) |  58 (45) | 32 (44) |  |
|  Elevated (≥223 IU/L) |  71 (55) | 40 (56) |  |
|  Not examined |  1 (1) |  |  |
| Peripheral blood lymphocyte count |  |  | 0.728 |
|  ≥1000/mL | 100 (77) | 54 (75) |  |
|  <1000/mL |  28 (22) | 17 (24) |  |
|  Not examined |  2 (2) | 1 (1) |  |
| Treatment |  |  | 0.871 |
|  Chemotherapy |  94 (72) | 51 (71) |  |
|  Best supportive care only |  36 (28) | 21 (29) |  |
| Chemotherapy regimen |  |  | 0.786 |
|  Platinum-based doublet or triplet |  74 (79) | 38 (75) |  |
|  Cytotoxic monotherapy |  12 (13) |  8 (16) |  |
|  Molecularly-targeted therapy |  8 (9) |  5 (10) |  |
| Abbreviations: CUP, cancer of unknown primary site; ECOG, Eastern Cooperative Oncology Group; CNS, central nervous system; LDH, lactate dehydrogenase. |
| aPercentages may not add up to 100 because of rounding. |
| bFisher’s exact test. |
| cCurrent smokers were defined as individuals who had smoked ≥100 cigarettes including at least one within the year prior to diagnosis; former smokers as those who had smoked ≥100 cigarettes but had quit >1 year prior to diagnosis; and never-smokers as those who had smoked <100 cigarettes. |
| dAdenosquamous, *n* = 3; not otherwise specified, *n* = 7. |
| eAdenosquamous, *n* = 1; not otherwise specified, *n* = 2. |