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1. Shi Y, Au JS, Thongprasert S, et al. A prospective, molecular epidemiology study of EGFR mutations in Asian patients with advanced non-small-cell lung cancer of adenocarcinoma histology (PIONEER). *J Thorac Oncol* 2014;9:154–162.
2. Ou SH, Ziogas A, Zell JA. A comparison study of clinicopathologic characteristics of Southern California Asian American Non-small Cell Lung Cancer (NSCLC) patients by smoking status. *J Thorac Oncol* 2010;5:158–168.

In Response:

Dr. Ou has requested smoking status by country/region, and by sex within each country/region, for the patients with advanced non–small-cell lung cancer (NSCLC) who were included in a molecular e*PI*demi*O*logy study in Asian patients with advanced *N*SCLC of ad*E*no histology to assess epidermal growth factor receptor (*EGFR*) mutation status (PIONEER) (NCT01185314), which analyzed data from 1482 eligible patients with advanced NSCLC.[1] We are pleased to supply below the subgroup analyses of smoking status data by country/region and by sex within each country/region in reply to Dr. Ou's request (Tables 1–3).

Dr. Ou et al. previously published that Vietnamese-American females with NSCLC had the highest proportion of never-smokers (65.5%) among the six Asian-American subgroups analyzed in their study, whereas Japanese-American females with NSCLC had the lowest proportion of never-smokers (19.3%).[2] In the

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PIONEER study, just more than half of all patients were never-smokers (52.6% [$n = 779/1482$]) and just more than one-fifth were regular smokers (22.1% [$n = 327/1482$]). Of the seven Asian countries/regions included in the PIONEER study, Taiwan had the greatest proportion of never-smokers (65.7%) and Vietnam had the lowest proportion of never-smokers (31.4%). Similarly, Taiwanese females with NSCLC had the highest proportion of never-smokers (97.8%) and Vietnamese males had the lowest proportion of never-smokers (12.9%) of all the sex subgroups analyzed.[1]

Dr. Ou et al. observed driver mutations in *EGFR*, anaplastic lymphoma kinase (*ALK*), gene encoding the proto-oncogene tyrosine-protein kinase ROS enzyme (*ROS1*), and RET proto-ocogene (*RET*) primarily in never-smokers.[2] In the PIONEER study, *EGFR* mutation status was evaluable in tumors from 1450 of 1482 patients (97.8%). By country, *EGFR* mutation frequency was highest in patients from Vietnam (64.2% [$n = 77$ of 120]) and lowest in patients from India (22.2% [$n = 16$ of 72]). Females had higher *EGFR* mutation frequency than males (61.1% [$n = 384$ of 628] and 44.0% [$n = 362$ of 822], respectively) across all countries. Considering smoking history, *EGFR* mutation frequency was highest among never-smokers (60.7% [$n = 462$ of 761]) compared with exsmokers (43.2% [$n = 130$ of 301]), occasional smokers (51.6% [$n = 33$ of 64]), or regular smokers (37.3% [$n = 121$ of 324]). *EGFR* mutation frequency was decreased as pack-year number increased (>0–10 pack-years: 57.9%; >50 pack-years: 31.4%). A similar trend was observed by sex: males (0–10 pack-years: 55.9% [$n = 161$ of 288], >10–30 pack-years: 46.6% [$n = 123$ of 264], >30 pack-years: 28.2% [$n = 74$ of 262]); females

(0–10 pack-years: 62.5% [$n = 371$ of 594], >10–30 pack-years: 37.5% [$n = 9$ of 24], >30 pack-years: 40.0% [$n = 4$ of 10]). PIONEER researchers concluded that a patient's ethnicity and smoking status/pack years were independent predictive factors for tumor *EGFR* mutation status. Other mutations were not explored in PIONEER.[1]

Given the limited sample sizes of these PIONEER subgroup analyses of smoking status data by country/region and by sex, we note that interpretation needs to be with caution, as the analyses may be subject to large sampling fluctuations. We thank Dr. Ou for his congratulations and interest in our study and hope the above is informative and useful for him and other interested parties.

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TABLE 1. Smoking History by Country (PP Population)

Smoking History	Total (*n* = 1482)	China (*n* = 7 47)	Hong Kong (*n* = 170)	India (*n* = 81)	Philippines (*n* = 66)	Taiwan (*n* = 178)	Thailand (*n* = 119)	Vietnam (*n* = 1 21)
Smoking[a], *n* (%)								
Never-smoker	779 (52.6)	421 (56.4)	77 (45.3)	47 (58.0)	36 (54.5)	117 (65.7)	43 (36.1)	38 (31.4)
Exsmoker	310 (20.9)	136 (18.2)	29 (17.1)	26 (32.1)	15 (22.7)	32 (18.0)	52 (43.7)	20 (16.5)
Occasional smoker	66 (4.5)	19 (2.5)	14 (8.2)	0	1 (1.5)	7 (3.9)	6 (5.0)	19 (15.7)
Regular smoker	327 (22.1)	171 (22.9)	50 (29.4)	8 (9.9)	14 (21.2)	22 (12.4)	18 (15.1)	44 (36.4)
Pack-years, *n* (%)								
0–10	902 (61.2)	470 (63.1)	89 (52.7)	51 (63.8)	39 (59.1)	126 (71.2)	68 (57.1)	59 (50.0)
>10–30	291 (19.7)	153 (20.5)	31 (18.3)	6 (7.5)	7 (10.6)	25 (14.1)	31 (26.1)	38 (32.2)
>30	281 (19.1)	122 (16.4)	49 (29.0)	23 (28.8)	20 (30.3)	26 (14.7)	20 (16.8)	21 (17.8)
Unknown	8	2	1	1	0	1	0	3

[a]Smoking history definitions: never-smoker (patients who had never smoked cigarettes in their lifetime); exsmoker (patients who had previously smoked but no longer smoked); occasional smoker (patients who smoked, but not every day); regular smoker (patients who smoked every day).

PP, per protocol.

TABLE 2. Smoking History by Country in Male Patients (PP Population)

Smoking History	Total (*n* = 839)	China (*n* = 397)	Hong Kong (*n* = 106)	India (*n* = 51)	Philippines (*n* = 39)	Taiwan (*n* = 86)	Thailand (*n* = 67)	Vietnam (*n* = 93)
Smoking[a], *n* (%)								
Never-smoker	188 (22.4)	92 (23.2)	20 (18.9)	18 (35.3)	10 (25.6)	27 (31.4)	9 (13.4)	12 (12.9)
Exsmoker	285 (34.0)	128 (32.2)	26 (24.5)	25 (49.0)	15 (38.5)	32 (37.2)	39 (58.2)	20 (21.5)
Occasional smoker	62 (7.4)	17 (4.3)	13 (12.3)	0	1 (2.6)	7 (8.1)	6 (9.0)	18 (19.4)
Regular smoker	304 (36.2)	160 (40.3)	47 (44.3)	8 (15.7)	13 (33.3)	20 (23.3)	13 (19.4)	43 (46.2)
Pack-years, *n* (%)								
0–10	294 (35.4)	136 (34.4)	31 (29.5)	22 (44.0)	13 (33.3)	36 (42.4)	24 (35.8)	32 (35.6)
>10–30	267 (32.1)	140 (35.4)	28 (26.7)	5 (10.0)	7 (17.9)	25 (29.4)	24 (35.8)	38 (42.2)
>30	270 (32.5)	119 (30.1)	46 (43.8)	23 (46.0)	19 (48.7)	24 (28.2)	19 (28.4)	20 (22.2)
Unknown	8	2	1	1	0	1	0	3

[a]Smoking history definitions: never-smoker (patients who had never smoked cigarettes in their lifetime); exsmoker (patients who had previously smoked but no longer smoked); occasional smoker (patients who smoked, but not every day); regular smoker (patients who smoked every day).

PP, per protocol.

TABLE 3. Smoking History by Country in Female Patients (PP Population)

Smoking History	Total (*n* = 643)	China (*n* = 350)	Hong Kong (*n* = 64)	India (*n* = 30)	Philippines (*n* = 27)	Taiwan (*n* = 92)	Thailand (*n* = 52)	Vietnam (*n* = 28)
Smoking[a], *n* (%)								
Never-smoker	591 (91.9)	329 (94.0)	57 (89.1)	29 (96.7)	26 (96.3)	90 (97.8)	34 (65.4)	26 (92.9)
Exsmoker	25 (3.9)	8 (2.3)	3 (4.7)	1 (3.3)	0	0	13 (25.0)	0
Occasional smoker	4 (0.6)	2 (0.6)	1 (1.6)	0	0	0	0	1 (3.6)
Regular smoker	23 (3.6)	11 (3.1)	3 (4.7)	0	1 (3.7)	2 (2.2)	5 (9.6)	1 (3.6)
Pack-years, *n* (%)								
0–10	608 (94.6)	334 (95.4)	58 (90.6)	29 (96.7)	26 (96.3)	90 (97.8)	44 (84.6)	27 (96.4)
>10–30	24 (3.7)	13 (3.7)	3 (4.7)	1 (3.3)	0	0	7 (13.5)	0
>30	11 (1.7)	3 (0.9)	3 (4.7)	0	1 (3.7)	2 (2.2)	1 (1.9)	1 (3.6)

[a]Smoking history definitions: never-smoker (patients who had never smoked cigarettes in their lifetime); exsmoker (patients who had previously smoked but no longer smoked); occasional smoker (patients who smoked, but not every day); regular smoker (patients who smoked every day).

PP, per protocol.