P3.002: Humidifier Use and CNS Progression During EGFR-TKI in EGFR-Mutated Lung Cancer: Korean EGFR Registry

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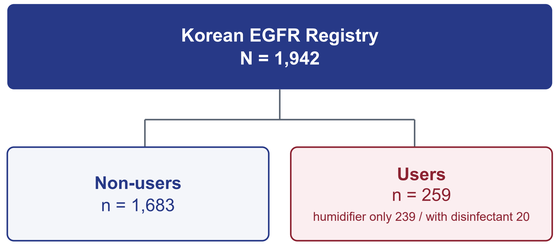
IASLC 2026 World Conference on Lung Cancer
SEPTEMBER 12 – 15, 2026
SEOUL, REPUBLIC OF KOREA

INTRODUCTION

- ***EGFR*-mutated lung cancer**
 - Well-established targeted therapies
 - But, Central nervous system → Common site of progression
- **Household humidifier -** Highly used in South Korea
 - Humidifier disinfectant exposure
 - Severe pulmonary toxicity
 - **Elevated lung cancer risk** (with a duration–response relationship)
 - **Polyhexamethylene guanidine induces lung tumors** (in rodent models)
 - **Whether this exposure influence the course of *EGFR*-mutated lung cancer is unknown.**
- **Objective**
 - To evaluate the association between humidifier-use and disease characteristics, metastatic patterns, and CNS metastasis risk during EGFR-TKI therapy.

METHODS

- **Design**
 - Korean EGFR Registry — multicenter retrospective cohort of patients with EGFR-mutated lung cancer across institutions in South Korea.
- **Exposure definition**
 - Self-reported household humidifier use.
 - Users = use for ≥5 years and ≥5 days/week
 - Non-users = all others.



- **Endpoints**
 - **Primary: New CNS metastasis during first-line EGFR-TKI**
 - Secondary
 - Metastasis at diagnosis, EGFR mutation subtypes, PD-L1 expression, Best overall response, and progression type
- **Statistics**
 - Chi-square and Fisher's exact tests for categorical variables; t-tests for continuous variables.

DISCUSSION & CONCLUSION

- **Key findings**
 - Humidifier users developed new CNS metastasis about **2.5 times more often** during first-line EGFR-TKI, and more often required whole-brain radiotherapy.
 - Users showed a distinct profile at diagnosis: higher T790M, lower PD-L1 ≥50% expression, and more frequent pericardial metastasis.
 - Response to EGFR-TKI was comparable, and the overall distribution of progression type did not reach significance.
- **Actionable take-away message**
 - A humidifier exposure history may identify patients who warrant closer CNS surveillance during EGFR-TKI therapy.
- **Limitations**
 - Retrospective design and self-reported exposure. Humidifier use was correlated with housing type (apartment residence 56.0% vs 42.5%), and the number of CNS events among users was small.
- **Future direction**
 - Prospective studies with multivariable adjustment, defined brain imaging surveillance, and mechanistic work on CNS tropism.

REFERENCES & ACKNOWLEDGEMENTS

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Acknowledgements

We thank the Korean EGFR Registry investigators and the patients who participated in this study.

- **Artificial Intelligence (AI) Use Disclosure**
- **Disclosure for this poster:** Anthropic Claude was used for language editing and layout preparation. It was not used to generate, analyse, or interpret study data. All scientific content was created and verified by the authors.

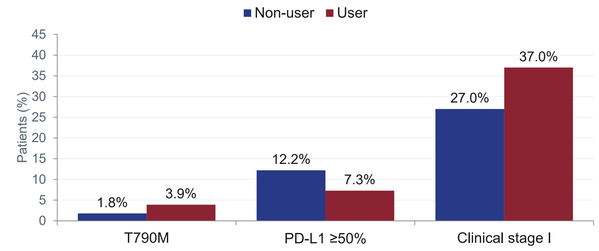
RESULTS

Table 1. Baseline, molecular and stage characteristics

Variable	Non-user (n=1,683)	User (n=259)	p
Age, yr, median [IQR]	69 [62–76]	65 [58–73]	**<0.001**
Female, n (%)	1,000 (59.4)	167 (64.5)	0.139
Never smoked, n (%)	1,080 (64.5)	166 (64.1)	0.526
Pack-years, mean (SD)	9.6 (17.9)	8.7 (15.1)	0.426
ECOG PS 0–1, n (%)	1,404 (92.7)	220 (96.1)	0.080
Apartment residence, n (%)	715 (42.5)	145 (56.0)	**<0.001**
Adenocarcinoma, n (%)	1,628 (96.7)	253 (97.7)	0.270
EGFR Ex19del, n (%)	802 (47.7)	129 (49.8)	0.562
T790M, n (%)	30 (1.8)	10 (3.9)	**0.050**
PD-L1 ≥50%, n (%)	205 (12.2)	19 (7.3)	**0.030**
Clinical stage I, n (%)	454 (27.0)	95 (37.0)	**0.008**

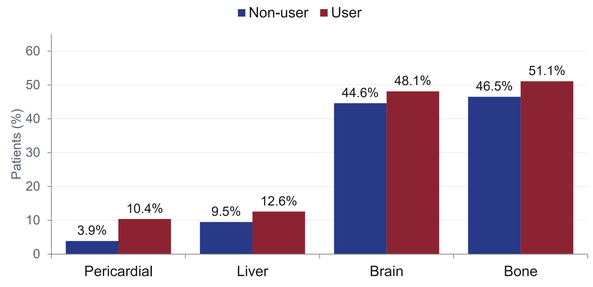
Users: humidifier use ≥5 years and ≥5 days/week. Bold p-values indicate p<0.05.

Figure 1. Distinct molecular and stage profile in humidifier users



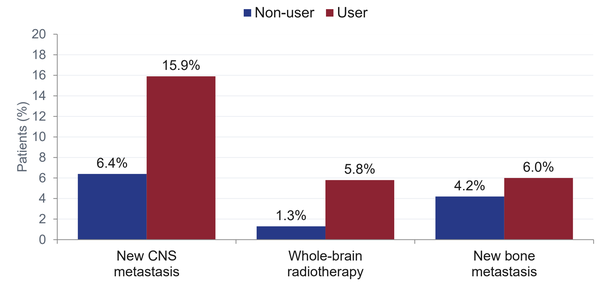
T790M p=0.050 · PD-L1 ≥50% p=0.030 · Clinical stage I p=0.008

Figure 2. Organ-specific metastasis at diagnosis (stage IV, N=1,108)



Pericardial p=0.002 · Liver p=0.321 · Brain p=0.494 · Bone p=0.356

Figure 3. Events during first-line EGFR-TKI therapy



New CNS metastasis p=0.010 · WBRT p=0.034 · New bone metastasis p=0.742

Best response and progression pattern (stage IV)

Outcome	Non-user	User	p
Objective response, CR+PR (N=1,025)	610/895 (68.2%)	89/130 (68.5%)	0.944
CNS progression (N=616 with documented type)	111/537 (20.7%)	23/79 (29.1%)	0.089

KEY MESSAGE

Household humidifier use was associated with a **2.5-fold higher rate of new CNS metastasis** during first-line EGFR-TKI (15.9% vs 6.4%, p=0.010) and a greater need for whole-brain radiotherapy (5.8% vs 1.3%, p=0.034), despite an **earlier stage at diagnosis** and comparable overall response.

- **Interpretation**
 - Humidifier users presented younger, at an earlier stage, and with better baseline quality of life, yet went on to develop new CNS metastasis more than twice as often during first-line EGFR-TKI and required whole-brain radiotherapy more frequently.
 - The accompanying molecular differences — higher T790M prevalence and lower PD-L1 expression — together with more frequent pericardial metastasis suggest that humidifier exposure may mark a biologically distinct disease with greater CNS tropism.
 - Because exposure was self-reported and correlated with housing type, prospective studies with multivariable adjustment are needed to validate these observations.