Results:
Among all patients, adenocarcinoma surpassed squamous cell carcinoma by 1975-1979. Adenocarcinoma rose 38% in men from 1980-1984, although this did not occur among blacks for another decade. Adenocarcinoma surpassed squamous cell carcinoma, small cell carcinoma, and large cell carcinoma in 1985-1989 in men, while adenocarcinoma increased sharply, and became strongly related to smoking.

Methods:
SEER data on 307,797 lung cancer patients diagnosed in the US between 1975 and 2003 were analyzed. The objective was to assess changes in age-standardized incidence rates (per 100,000 population) at diagnosis of the four major lung cancer histologies: adenocarcinoma, squamous cell carcinoma, small cell carcinoma, and large cell carcinoma. Incidence of each histologic subtype was measured during six time periods (1975-1979, 1980-1984, 1985-1989, 1990-1994, 1995-1999, and 2000-2003). Comparisons were drawn based upon gender, race, and age. Because SEER contains no data on cigarette smoking, other sources were utilized to correlate changing histology to time trends in smoking prevalence, the changing cigarette, and Tobacco Institute actions.

Results:
Among all patients, adenocarcinoma surpassed squamous cell carcinoma by 1980-1984 to become the most common histologic subtype. The incidence of adenocarcinoma rose 62% between 1975-1979 and 1995-1999, but then fell 8% in 2000-2003. Squamous cell carcinoma incidence peaked in 1980-1984 and dropped by 35% by 2000-2003. Adenocarcinoma surpassed squamous cell in 1985-1989 in men, while adenocarcinoma had already become the most common form of lung cancer in women by 1975-1979. Adenocarcinoma rose 38% in men from 1975-1979 to 1995-1999, while it doubled in women during this interval. Among whites, adenocarcinoma surpassed squamous carcinoma by 1980-1984, although this did not occur among blacks for another decade. Nonetheless, incidence rate of adenocarcinoma has consistently been significantly higher among black males than in other subgroups, while incidence of adenocarcinoma has been nearly identical among white and black women. Adenocarcinoma was already most common among patients ≤50 yrs of age by 1975-1979, while adenocarcinoma rapidly increased and surpassed squamous carcinoma in all other age groups by 1990-1994. By 2000-2003, adenocarcinoma comprised 47% of all lung cancers (42% in men; 52% in women; 59% in pts <50 yrs). Currently, adenocarcinoma is the most common histology in both sexes, races, and in all age groups.

Conclusions:
The dramatic rise of adenocarcinoma of the lung is consistent with the hypothesis that changes in cigarette design and composition were the major factors that were responsible for this rise. This increase has been most striking among women and younger persons. Trends in adenocarcinoma correlate with the wide-scale adoption by smokers of filtered and low tar cigarettes, and with increasing nitrosamine levels in cigarettes. While filtered cigarettes comprised only 1% of the market in 1950, their use rapidly increased to 64% in 1964 and 95% in 1986. Today 98% of cigarettes made in the US are filtered. Specifically, the use of filter vents in cigarette design likely played a substantial role in this rapid rise of adenocarcinoma of the lung. The use of filter vents reduces the resistance to draw allowing smokers to take bigger, deeper puffs thereby facilitating the delivery of smoke particles deep into the airways. These changes were introduced by the Tobacco Industry in response to mounting evidence that cigarette smoking caused other forms of lung cancer. These actions by the Tobacco Industry contributed to the development of an epidemic of smoking-related adenocarcinoma of the lung.

PRS-02
Gefitinib (IRESSA) versus docetaxel in patients with locally advanced or metastatic non-small-cell lung cancer pre-treated with platinum-based chemotherapy: a randomized, open-label Phase III study (INTEREST)

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Background:
This Phase III, randomized, open-label, multicenter, parallel-group study (INTEREST [IRESSA non-small-cell lung cancer (NSCLC) Trial Evaluating REsponse and Survival against Taxotere]), compared gefitinib with docetaxel in patients with locally advanced or metastatic NSCLC pretreated with platinum-based chemotherapy. This is the largest reported Phase III study comparing targeted therapy (gefitinib) with chemotherapy (docetaxel).

Methods:
Patients (≥18 years, performance status [PS] 0-2) with locally advanced or metastatic NSCLC who had progressed or recurred following 1 or 2 prior chemotherapy regimens (at least 1 platinum-based) were randomized to receive gefitinib (250 mg/day orally) or docetaxel (75 mg/m² iv every 3 weeks). The primary objective was to compare overall survival between gefitinib and docetaxel using a co-primary analysis in both the overall population (non-inferiority) and, as a protocol amendment following the emergence of biomarker data, in patients with high epidermal growth factor receptor (EGFR) gene copy number (measured by fluorescence in situ hybridization) (superiority). Secondary endpoints were progression free survival, objective response rate (assessed by RECIST), patient-reported functionality and quality of life (measured using the Functional Assessment of Cancer Therapy-Lung total score, trial outcome index and lung cancer subscale), and safety and tolerability (according to Common Toxicity Criteria version 2.0). Exploratory endpoints including other biomarkers and quality of life endpoints were also assessed. A Cox proportional hazards model analysis adjusting only for randomized treatment was used to compare overall survival between the randomized treatments.