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## Lung cancer in young females

To the Editor:

We read with interest the article by LIENERT *et al.* [1]. Based on data of the clinical cancer registry at the Lungenklinik Heckeshorn, Berlin, 1986–1995, the authors examined whether young female lung cancer patients ( $\leq 45$  yrs of age,  $n=96$ ) differ from all other lung cancer patients ( $n=4,843$ ) with respect to risk factors, histology and clinical features. They found a higher proportion of adenocarcinomas (38%) and carcinoids in young females. Other main characteristics of young females were a high proportion of ever-smokers (88%) and a large number of patients who reported a first degree relative with lung cancer (13%). We would like to add our recent findings of a large-scaled, case-control study of lung cancer conducted in Germany from 1990–1996 [2, 3], which aimed to investigate risk factors for lung cancer in young adults. This study included 251 young patients and 280 population controls ( $\leq 45$  yrs of age), as well as 2,009 older cases and 2,039 older controls (55–69 yrs of age). Adenocarcinomas were more frequent in young males (41%) and young and older females (44% and 47%, respectively) than in older males (28%). Differences in histology between age groups could be explained, in part, by differences in smoking patterns. However, there are still unknown factors that appear to favour the development of adenocarcinoma in the young [3]. A history of lung cancer in first degree relatives was associated with a 2.6-fold (95% confidence interval (CI) 1.1–6.0) increased risk in the young, while no elevated risk was observed in the older group (odds ratio=1.2 95% CI 0.9–1.6). Additional evidence for an age-specific genetic predisposition in lung cancer was recently provided by GAUDERMAN and MORRISON [4]. About 80% of our young female cases were current smokers, demonstrating a 30-fold increased lung cancer risk compared to never-smoking young females [2]. As stated by

LIENERT *et al.* [1], smoking is the main risk factor for lung cancer in young females. This was recently supported in a pooled analysis of European case-control studies of lung cancer in young females [5], where 84% of female patients aged 40–45 yrs could be attributed to active smoking.

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From the authors:

The valuable data of our colleagues M. Kreuzer and H.E. Wichmann support the main results from our own series. Yet it is remarkable that in their patients, adenocarcinoma in older females (55–69 yrs of age)

was even more frequent than in young female patients, in contrast to the predominance of adenocarcinoma in young females in our series. Regional differences could be assumed. A genetic component in the evolution of lung cancer in young patients has already been described [1], leading to an ongoing prospective study on this subject, conducted by H.E. Wichmann and with the participation of our hospital.

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## Long-term treatment of pulmonary hypertension with aerosolized iloprost

To the Editor:

MACHHERNDL *et al.* [1] report that long-term treatment of pulmonary hypertension with aerosolized iloprost was ineffective in a group of 12 patients with pulmonary arterial hypertension. These authors as well as GALIE [2] in an accompanying editorial state that the patients in this study were comparable to the patients in whom our group has recently reported favourable long-term effects of aerosolized iloprost [3]. We believe that this is not the case. The patients in our study suffered exclusively from primary pulmonary hypertension [3]. The study by MACHHERNDL *et al.* [1], in contrast, included only one patient with primary pulmonary hypertension. Five of their patients suffered from chronic thromboembolic pulmonary hypertension and six patients from Eisenmenger's syndrome. Although our experience with the therapeutic use of inhaled iloprost in patients with these forms of pulmonary hypertension is only limited, the report by MACHHERNDL *et al.* [1] supports our own impression that aerosolized iloprost is far less effective in these settings than in primary pulmonary hypertension.

We also agree with GALIE [2] that the results of controlled clinical trials should guide treatment of pulmonary arterial hypertension. However, all controlled clinical trials in pulmonary hypertension have studied the effects of new treatment modalities for a few months only. We have not learned anything from these trials about the long-term effects of the treatments that we now routinely apply to patients. Since long-term placebo controlled trials are unethical in a deadly disease, observational follow-up studies are a useful and necessary means to obtain at least some information about the long-term effects of new treatments.

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From the authors:

We value GALIE's [1] and HIGENBOTTAM's [2] editorial comments surrounding our report on the long-term treatment of pulmonary hypertension with aerosolized iloprost [3], and we appreciate M.M. Hoepfer's recent comments. M.M. Hoepfer points out that the apparent disagreements between his data [4] and our report may be due to the differences in the patient populations. We agree with him entirely. We have pointed out the fundamental differences in the patient populations in the discussion section of our manuscript. However, M.M. Hoepfer states that six of our patients suffered from Eisenmenger's syndrome. This is not correct. As outlined in table 1 of our manuscript, two of the four patients with pulmonary hypertension related to congenital systemic pulmonary shunts had had prior surgical corrections with no residual shunts, while the other two had left-to-right shunts and were not Eisenmenger patients. Furthermore, we believe that differences in clinical status did indeed have a bearing on the study outcome rather than differences in diagnoses. While M.M. Hoepfer's patients were on average 10 yrs younger than our patients, with five >50% haemodynamic responders and twelve >20% haemodynamic responders, there were only two patients in our study who demonstrated a >20% decrease in both pulmonary vascular resistance and mean pulmonary arterial pressure. Taken together, we treated sicker patients. In the pulmonary hypertension clinical outpatient unit at our institution, old inoperable patients with chronic thromboembolic pulmonary hypertension are the most frequent referral. In these patients, one would