

## Miliary Metastases are Associated with Epidermal Growth Factor Receptor Mutations in Non-Small Cell Lung Cancer

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**Categories:** Radiation Oncology

**Keywords:** egfr, miliary, lung cancer, metastases

### How to cite this poster

Hsu F, Toriumi T, De Caluwe A (2016) Miliary Metastases are Associated with Epidermal Growth Factor Receptor Mutations in Non-Small Cell Lung Cancer. Cureus 8(8): e.

## Abstract

**Purpose:** Miliary metastases arise from widespread hematogenous disease dissemination and are characterized by metastatic nodules that are diffuse, innumerable and small. The purpose of this study was to examine the incidence, prognostic significance, and impact of epidermal growth factor receptor (EGFR) mutations for miliary metastases from non-small cell lung cancer (NSCLC).

**Materials:** Patients were identified from a Provincial cancer registry (British Columbia, Canada) for the years 2010-2012. Inclusion criteria were stage IV NSCLC at presentation and conclusive EGFR mutation testing. Miliary metastases were objectively defined as >15 metastatic nodules of < 1cm diameter size involving more than one organ lobe and bilaterally distributed. The primary endpoint was the incidence of miliary lung, brain, and liver metastases. Secondary endpoints were survival and the prognostic implication for each site of miliary metastases.

**Results:** For 543 patients, the total number of brain, lung, and liver metastases were 165 (30.4%), 290 (53.4%), and 67 (12.3%), respectively. The EGFR mutation positive (EGFR+) subgroup had a significantly higher 3-year cumulative incidence of miliary brain (4.1% vs. 1.4%,  $p = 0.015$ ) and miliary lung (11.6% vs. 3.3%,  $p < 0.001$ ) metastases compared to EGFR wild type. A higher proportion of metastases from EGFR+ cancers were miliary for brain (8.5% vs. 1.7%,  $p = 0.035$ ) and lung (18.9% vs. 6.9%,  $p = 0.003$ ) sites. Survival following the diagnosis of brain, lung, and liver metastases were 6.5, 11.9, and 4.3 months, respectively. Miliary metastases were not a significant factor for survival in EGFR+ or EGFR WT subgroups.

**Conclusions:** Mutations in EGFR are associated with a higher rate of miliary brain and lung metastases. Despite the remarkable radiographic presentation, patients with miliary metastases did not have worse survival outcomes compared to non-miliary metastases.

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Published 08/06/2016

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