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# Randomized Phase II Trial of Erlotinib or Standard Chemotherapy in Patients With Advanced Non–Small-Cell Lung Cancer and a Performance Status of 2

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R Lilenbaum *et al.* JCO. Feb 20 2008; 26(6):863-869

**Background:**
PS is the most important selection criterion for treatment of patients with advanced NSCL cancer. Most clinical trials now exclude PS 2 patients. A prior CALGB trial showed Carboplatin/ Paclitaxel to be superior to paclitaxel alone. BR 21 compared erlotinib to placebo in 2nd or 3rd line setting including patients with PS 2 or 3. BR 21 showed significant benefit of erlotinib over placebo. This trial was done to compare first line erlotinib to chemotherapy with carboplatin/ paclitaxel in unselected PS 2 patients.

**Study design:**
Randomized phase II; Primary end point PFS ( therapy considered ineffective if PFS < 2 months; worthy of further study if PFS > 3.5 months). Inclusion Criteria – confirmed NSCL cancer, 3B or 4, measurable or assessable disease, no prior chemo or EGFR inhibitor, stable brain mets off steroids, PS 2

Patients randomized to Erlotinib 150 mg per day until progression or Carbo/Paclitaxel (standard dose) for 4 cycles. Patients progressing on erlotinib treated at investigator's discretion. Patients progressing on, or intolerant of, chemo were to receive erlotinib.

**Study results:**
103 patients randomized, 86% stage 4, 46% at least 70 years old , smoking history same in both arms. More females in erlotinib.

| Efficacy | Erlotinib | Chemo | HR/p value |
|---|---|---|---|
| PFS | 1.9 mos | 3.5 mos | 1.45/ .063 |
| OS | 6.6 mos | 9.5 mos | 1.73 |
| RR | 4% | 12% | |

Subgroup analysis looking at clinical predictors limited by small numbers but males, squamous cell and smokers did much better with chemotherapy while females, adenocarcinoma and never smokers did slightly better with erlotinib.
Subgroup analysis based on molecular markers limited by even smaller numbers but EGFR positivity by IHC or FISH both did better with chemotherapy.

**Study commentary:**
This is the first attempt at a randomized trial of first line erlotinib versus standard chemo in PS 2 patients. The study population was not enriched for EGFR TKI responders. IN this setting chemotherapy appears to be a better first line option than erlotinib. In clinical

subgroups less likely to respond to TKI (male, smoker, squamous,) chemo was clearly better. Even in those clinical groups more likely to respond to a TKI (female, adeno, never smoker) erlotinib was not much better than chemo except perhaps in never smokers.

**Bottomline for Canadian medical oncologists:**
Erlotinib is approved (and funded) in the second or third line setting. However, medical oncologists are often faced with patients of borderline PS (PS 2) for whom we are reluctant (or the patient is reluctant) to use chemotherapy. The temptation is to offer these patients erlotinib first line especially if the patient has coverage for the drug or wishes to pay out of pocket. This study, although limited by phase II nature, suggests that we should resist the temptation to use first line erlotinib.