

Background

- **The NCIC CTG BR.21 trial:**
 - OS, PFS, RR and QoL superior in erlotinib arm
- **Predictors of response**
 - Clinical: female gender; adenocarcinoma; never smoker status; Asian ethnicity
 - Molecular: EGFR protein expression; *EGFR* gene copy number; *EGFR* TK domain gene mutation status; *K-ras* gene mutation status
- **Cost effectiveness analysis of erlotinib**
 - Incremental cost effectiveness ratio (ICER)
$$\frac{\text{Mean Cost A} - \text{Mean Cost B}}{\text{Mean Survival A} - \text{Mean Survival B}}$$
 - ICER of erlotinib is \$ 95,869 CAD/ life year gained (LYG)

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Aims/ Methods

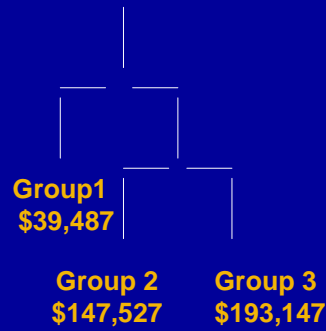
- **Aims**
 - To investigate methodology utilizing combinations of multiple predictors of response to identify more and less cost effective sub-groups of patients, that can be utilized in cost effectiveness analyses in the future
 - To apply this methodology to the NCIC CTG BR.21 trial database
- **Three methodologies:**
 - Classification and regression tree (CART) analysis based on net benefits to ID subgroups with different ICERs
 - Net monetary benefit regression model based on 3 willingness to pay thresholds for an additional effect
 - Calculation of ICERs over all potential subgroups using covariates to identify highest and lowest ICERs

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Results: Classification and Regression Tree Analysis Based on Net Benefits

- Group 1-Non-smokers (n=83; ICER=\$39,487)
- Group 2- Current/ Past smokers/ *EGFR* mutation (n=21; ICER=\$147, 527)
- Group 3- Current/ Past smokers with wildtype
- *K-ras* (n=127; ICER=\$193, 147)



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Results: Characteristics that predict for different net benefits by treatment

Willingness to pay	Characteristics (clinical and molecular) with p<0.1 for interaction with treatment
\$50,000/ LYG	Ethnicity (p=0.050) <i>EGFR</i> gene mutation (p=0.025) Histology (p=0.052) <i>EGFR</i> copy number (p=0.09)
\$75,000/LYG	Ethnicity (p=0.07) <i>EGFR</i> gene mutation (p=0.04) Histology (p=0.024) <i>K-ras</i> mutation (p=0.093) <i>EGFR</i> copy number (p=0.082)
\$100,000/LYG	Ethnicity (p=0.098) <i>EGFR</i> gene mutation (p=0.056) Histology (p=0.02) <i>K-ras</i> mutation (p=0.090) <i>EGFR</i> copy number (p=0.087)

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Conclusions

- We demonstrated clinical and molecular predictors have an important impact on cost effectiveness of erlotinib therapy
 - CART mirrored the clinical predictors subgroups
 - Regression of NMB addressing potential imbalance in subgroups despite initial randomization
 - Unable to identify best method
- Clinical data should continue to drive policy decisions
- However, if clinical benefit and cost effectiveness are modest:
 - Efforts to identify subgroups with greater clinical benefit should be supported
 - Improve access to novel therapies

