Applications of Cancer Pharmacogenomics in a Naturalistic Setting

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Naturalistic setting of Medco

- Supports PPWG preliminary recommendations

Retrospective database research possibilities

- Extend prior research
- Expand size, outcomes
- Supply information about ‘usual care’ patients

Prospective research/programs

- Adoption statistics – clinician, patients
- Population-based prevalence numbers

Relation to Comparative Effectiveness Research (CER)

"Compare the effectiveness of genetic and biomarker testing and usual care in preventing and treating breast cancer….."

Key Elements[1]

- Direct comparison of effective interventions
- Study of patients in typical day-to-day clinical care
- Aim to tailor decisions to the needs of individual patients

[1]Source: Institute of Medicine Report Brief June 2009: Initial national priorities for comparative effectiveness research

Naturalistic Setting of Medco

Pharmacy and a database system

- 2200 pharmacists serve ~8 million US lives
- Wired pharmacies (all 60,000) serve an additional ~ 55+ million US lives

On ~20 million lives – longitudinal data on hospitalizations, labs, visits, procedures and coding for diagnoses linked with prescription data

Retrospective study and Pharmacogenomics: Example of Phenocopying a genetic mutation

Increased risk of breast cancer recurrence in women initiating tamoxifen with CYP2D6 inhibitors

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Background

Hepatic cytochrome P450 2D6 (CYP2D6) is key in metabolic activation of tamoxifen to its active metabolite, endoxifen

Previous studies have shown that women receiving tamoxifen who have reduced-function CYP2D6 polymorphisms and are poor metabolizers have lower levels of endoxifen and higher recurrence rates

Previous small studies with CYP2D6 inhibitors and tamoxifen show reductions in endoxifen (45-58%), but have not delineated their impact on breast cancer recurrence

Study Design

Retrospective cohort analysis of medical and pharmacy claims from a 10 million-member Integrated Database (Medco Health Solutions, Inc)

- ICD-9 and CPT-4 codes

Study Population:

- Women who initiated tamoxifen therapy 07/01/2003 - 12/31/2005

Inclusion criteria:

- Continuously eligible 6-months prior to initiating tamoxifen
- Tamoxifen-naïve (6-month negative history)
- Tamoxifen persisting at least 24 months post-initiation and reasonable level of adherence (MPR ≥0.70)
- Diagnosis of breast cancer

CYP2D6 Inhibitor Exposure Cohorts

Cohort stratification based on therapy received at any time over initial 24 months of follow-up after initiating tamoxifen therapy determined to be a CYP2D6-inhibitor by any of 4 reference documents

No CYP2D6-inhibitor Exposure

- Patients with no prescription claim for a drug considered CYP2D6 inhibitor at anytime during the follow-up period

CYP2D6-inhibitor Exposure

- CYP2D6 inhibitor with overlapping days of therapy with tamoxifen

Primary End Point

Follow-up measurement starts 6-months post-initiation of therapy and continued through 12/31/2007

Hospitalization for breast cancer during the follow-up period (determined by ICD-9 and CPT-4 codes)

- Breast cancer diagnosis *or* one or more of the following procedures:
  - Lumpectomy
  - Partial mastectomy
  - Lymph node dissection
  - Mastectomy
  - Radiation therapy