Effects of Brand vs. Generic Immunosuppressants on Graft Failure among U.S. Liver Transplant Recipients:

Analysis of SRTR and Medicare Claims Data

Jarcy Zee, Ghalib Bello, Murewa Oguntimein, Qian Liu, Abigail Smith, Charlotte Beil, Jeong Park, Adam Saulles, Sangeeta Goel, Rajesh Balkrishnan, Melissa Fava, Robert Merion, Alan Leichtman, Pratima Sharma

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Introduction

- Generic immunosuppressant (IS) use for liver transplantation (LT) has increased in some countries following expiration of brand patents.
- Reports of risks and benefits of generic IS substitution have been inconsistent.
  - Bioequivalence requirements differ across countries.
  - Only small, short-term studies have examined the effects of substitution on transplant outcomes.
- Goal: compare effects of brand and generic tacrolimus on the long-term risk of graft failure in a large, national cohort of U.S. LT recipients

Study Sample

- Data Sources
  - Scientific Registry of Transplant Recipients (SRTR) for liver transplant recipient identification and graft failure events
  - Centers for Medicare & Medicaid Services (CMS), Part D claims for generic or brand IS prescriptions
- Inclusion Criteria
  - Liver transplant in 2008-2012
  - At least one Medicare Part D claim for tacrolimus prescription
  - Graft function 30 days after transplant

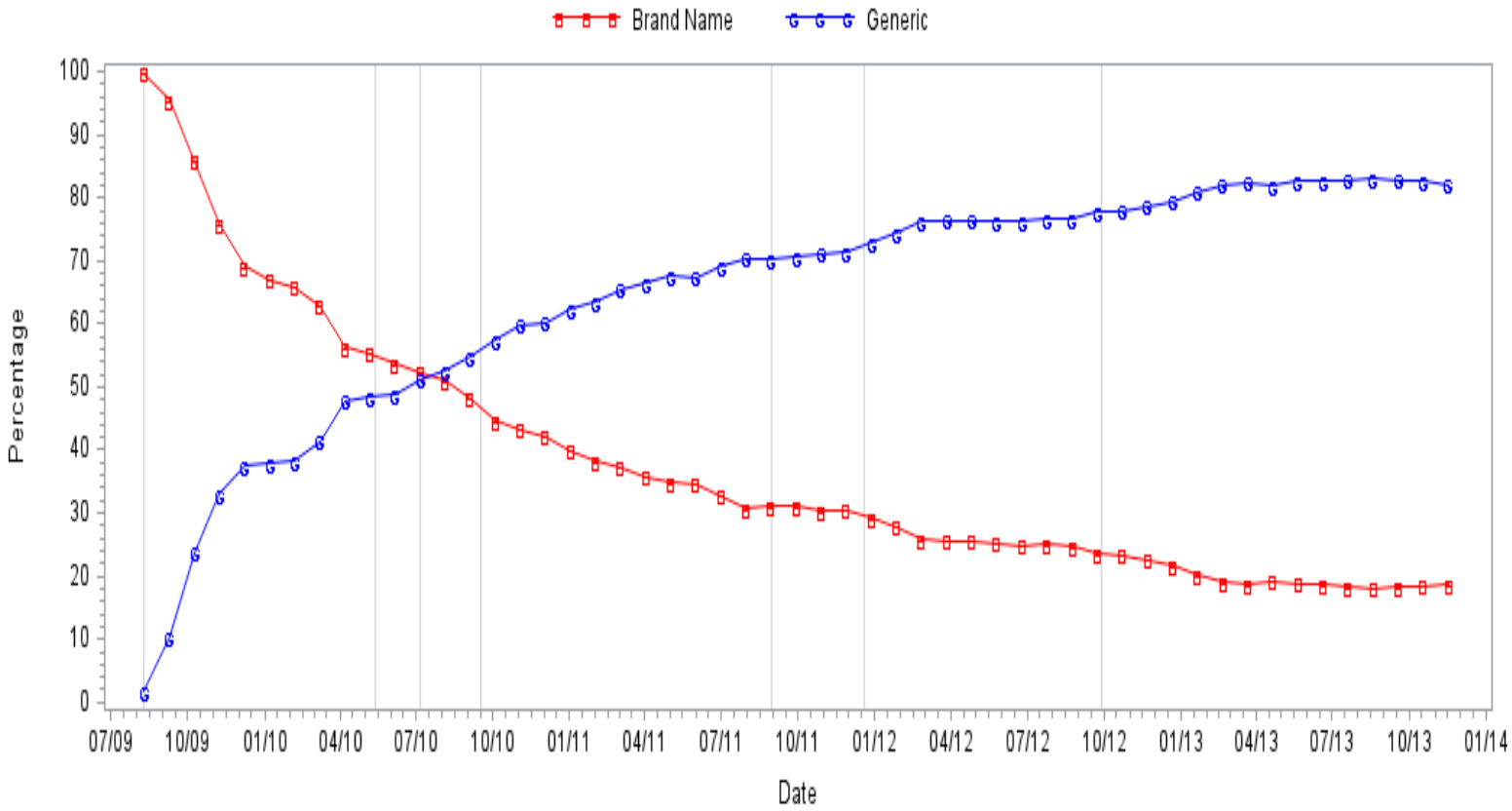
Statistical Methods

- Time-dependent Cox Proportional Hazards models
  - Generic vs. Brand status updated at each new claim
- Only consider time at risk when both brand and generic were available
- Model selection for adjustment covariates, including recipient and donor characteristics
- Sensitivity analyses excluded patients who ever switched from brand to generic or generic to brand

Cohort Characteristics

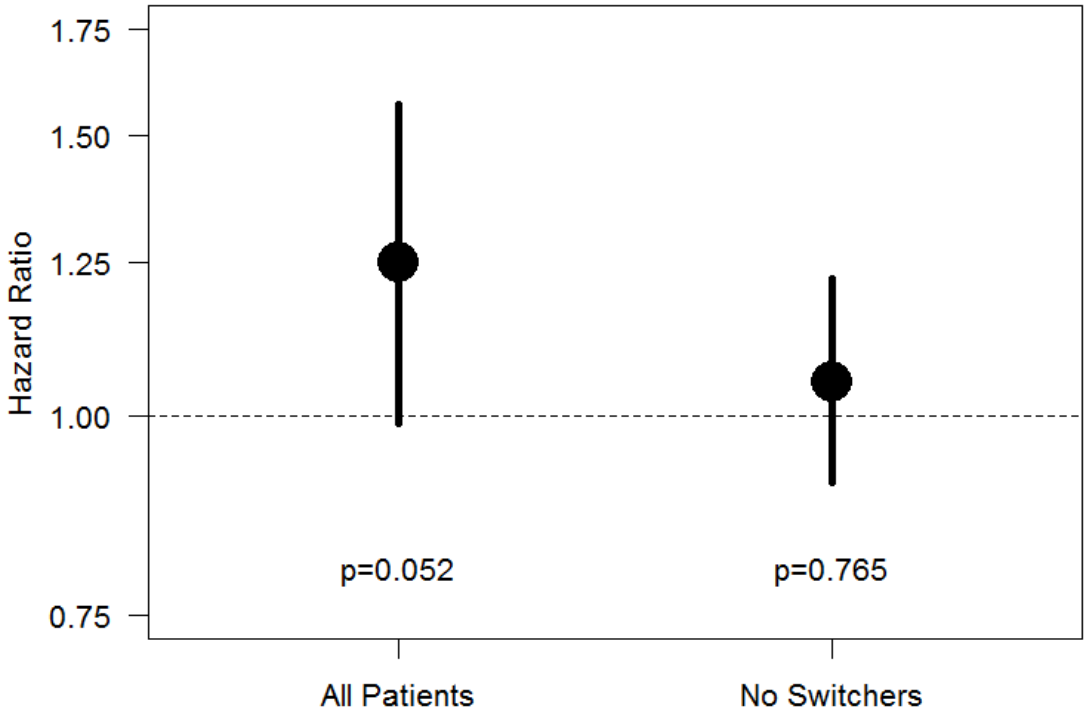
N	4169
Age, years, Mean (SD)	54.8 (10.0)
Male, % (N)	63.5 (2647)
Race/Ethnicity	
White	67.9 (2829)
Black	10.2 (425)
Asian/Other	5.5 (228)
Hispanic	16.5 (687)
BMI, Mean (SD)	28.5 (6.0)
Previous Liver Transplant, % (N)	5.2 (218)
Primary and Secondary Causes of Liver Disease, % (N)	
Non-Cholestatic Cirrhosis	50.2 (2093)
HCV	43.1 (1798)
Malignant Neoplasms	29.6 (1235)
Cholestatic Liver Disease/Cirrhosis	8.8 (365)
AHN	4.3 (181)
Metabolic Diseases	3.5 (144)
Other liver disease	14.1 (588)
Follow-up Time, years, Median (IQR)	3.8 (2.6-4.9)

Generic/Brand Tacrolimus Uptake Over Time



Model Results

Hazard ratios and 95% confidence intervals of graft survival comparing generic to brand IS



Each model stratified by transplant date and adjusted for recipient race, age, BMI, cause of end stage liver disease, donor age and type (deceased, living related, living unrelated)

Conclusions

- Among LT recipients with no evidence of switch between generic and brand IS, no significant difference in risk of long-term graft failure
- More research needed on effect of switching between brand and generic on graft survival
- Limitations
  - Number of Medicare Part D claims for each patient is low
  - Unknown generalizability to other U.S. or world-wide transplant populations
  - Adherence to prescriptions unknown