POST-MARKETING ADVERSE EVENTS OF ONCOLOGY MEDICATIONS WITH BREAKTHROUGH THERAPY DESIGNATION CORRELATED WITH TIME ON MARKET AND MARKET SHARE

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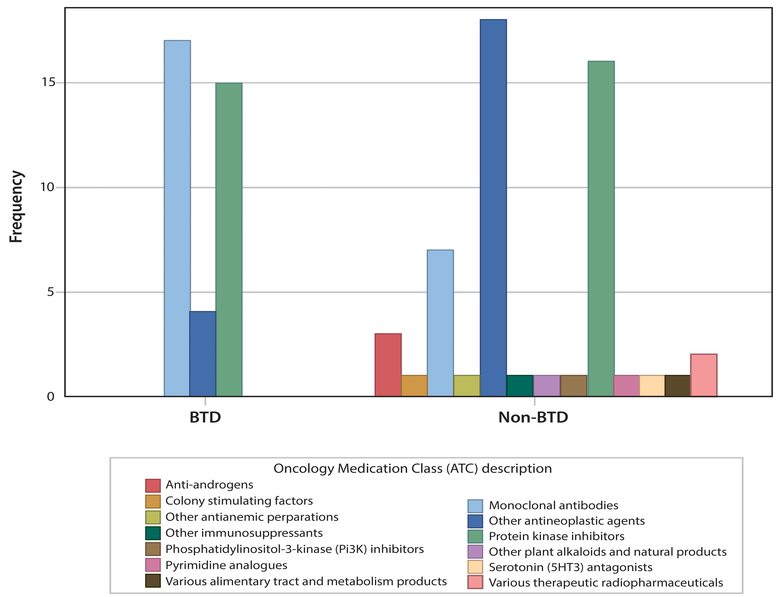
INTRODUCTION

We compare post-marketing adverse events (PMAEs) in oncology medications approved with Breakthrough Therapy Designation (BTD) vs. without BTD (Fig 1). BTD is an expedited drug pathway frequently used to bring oncology drugs to market. We study oncology treatments because in 2019 they amounted to $145.4 billion in US sales and accounted for the highest revenue of any other drug class.[1] Historically, oncology drugs have high rates of adverse events (AEs). However, previous studies have not found a significant difference in safety between BTD and non-BTD.[2,3]

Figure 1. BTD versus Non-BTD Oncology Medication Class 2012-2019



METHODOLOGY

- **Data Sources:** New drug applications (NDAs) from the Drugs@FDA database combined with PMAEs from the FDA Adverse Event Reporting System (FAERS) database.
- **Data Span:** 2012-2019
- **Death, and Annual PMAEs** from FAERS; Categorized as Total and Serious PMAEs
- **Market share** measured as publicly reported company earnings in 2019; Categorized as High (n=7), Medium (n=36), and Low (n=49) using quartiles. Descriptive average reported earning (in million): μ =808 σ =1454 IQR 610. Medium ~ 808 million. Negatively skewed distribution due to unreported earnings.
- **Time on Market** calculated as average time the drug was on market. Range: 0 (<0.5 year) – 7 years.
- **Research Method:** chi squared (X^2), ANOVA, and logistical regression using SAS.

RESULTS

- Oncology NDAs = 92. BTDs = 36/92 (39%); Non-BTDs = 56/92 (61%). (Fig 1).
- Logistical regression and X^2 test show no statistically significant differences in BTD vs Non BTD by drug class, date of release, and number of PMAEs reported per year on market.
- Including time on market as a covariate, shows BTD significantly associated with PMAEs.

Table 1 : PMAEs ANOVA main effect model with BTD, time on market, and market share

Total	F(4,85) = 13.7, p <0.0001
Serious	F(4,85) = 15.5, p <0.0001
Death	F(4,85) = 9.05, p <0.0001

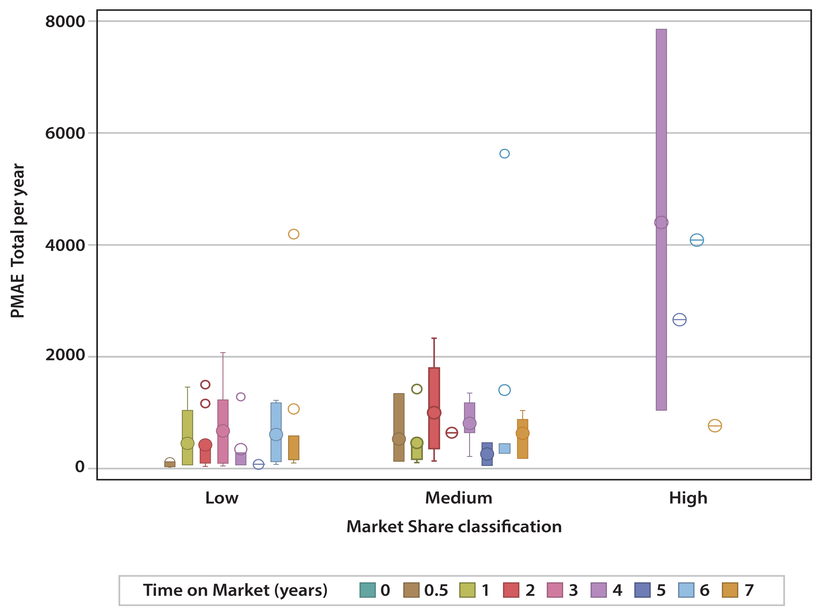
- ANOVA models including BTD, time on market, and market share are significant with Total and Serious PMAEs, and death (Table 1).

Table 2: ANOVA Model with BTD, time on market, and market share interaction term

PMAEs	BTD	Market Share
Total	$F(1,2) = 5.18$, $p < 0.025$	$F(1,2) = 23.7$, $p < 0.0001$
Serious	$F(1,2) = 6.8$, $p < 0.01$	$F(1,2) = 27.5$, $p < 0.0001$
Death	$F(1,2) = 3.88$, $p < 0.052$	$F(1,2) = 16.1$ $p < 0.0001$

- Death PMAE interaction with BTD $F(1,2) = 3.88$, $p < 0.052$, is marginally significant (Table 2).
- BTD and high market share is associated with Total PMAEs specifically for high market share t=6.06, $p < 0.001$ (Fig 2.) indicating an association with Total PMAEs.

Figure 2. Total PMAES with Market Share and Time on Market



LIMITATIONS

- PMAEs in FAERS data may be incomplete; include duplicated reports, unverified reports; inability to establish rates of occurrence; cannot establish causation.
- Market share data from publicly released financial earnings data may contain variations in reported numbers. Categorized to ordinal #s to overcome the issue.
- Time on Market estimated in years, which may affect medications <0.5 years.
- All data is cumulative, financial data from a single year of 2019.

CONCLUSIONS

- Oncology medications with BTD and high market share increase total PMAEs and serious PMAEs.
- Market share positively and significantly associated with all types of PMAEs
- BTD significance seems suppressed when time on market is omitted.
- **Implications related to** oncology medications:
  - BTD with high market share and longer time on market are more likely to have sufficient # of reported PMAEs to detect safety events, while
  - BTD with a low market share and low time on market do not.
  - Factors such as **time on market** and **market share** should be considered when examining the post-marketing adverse event profile of oncology medications.

REFERENCES

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