# Sacituzumab Govitecan Dosing and Neutropenia Risk in Patients with HER2-Negative Metastatic Breast Cancer

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## BACKGROUND

- Sacituzumab govitecan (SG) is a TROP2-directed antibody drug conjugate with topoisomerase I inhibitor payload which has demonstrated improved efficacy over standard chemotherapy in both HR-positive and triple-negative breast cancer
- **Neutropenia** represents a significant dose-limiting toxicity. Label updates in 2022-2023 shifted guidance to emphasize **primary G-CSF prophylaxis** for high-risk patients (≥65 years, previous neutropenia, poor performance status, organ dysfunction, or multiple comorbidities) versus secondary prophylaxis after neutropenic events develop. With increasing real-world use and varying dosing strategies, better understanding of dose-dependent toxicity patterns and the role of prophylactic supportive care is essential to optimize patient outcomes

## METHODS

- **Study Design:** Single-center retrospective cohort study
- **Population:** HER2-negative metastatic breast cancer patients receiving SG (April 2020 - December 2024)
- **Data Collected:** Patient demographics, disease characteristics, treatment patterns, safety outcomes including hospital admissions, and G-CSF use
- **Analysis:** Inverse probability weighting (IPW) based on propensity scores using logistic regression models to control for confounding variables (age, prophylactic G-CSF, number of prior lines of treatment, and starting dose). For variables with missing values, additional weight adjustments were incorporated to reduce potential bias

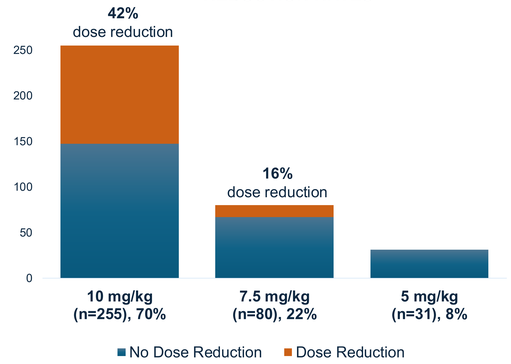
### PATIENT CHARACTERISTICS

| | 10 mg/kg | 7.5 mg/kg | 5 mg/kg | Total |
|---|---|---|---|---|
| **AGE AT START OF TREATMENT*** (YRS) | 54 (25-76) | 57 (24-82) | 57 (35-83) | 54 |
| **TREATMENT DURATION ON SG*** (DAYS) | 116 (0-1443) | 112 (7-476) | 50 (7-923) | 110 |
| **PRIOR METASTATIC TREATMENT LINES*** | 2 (0-10) | 2 (0-10) | 3 (1-16) | 2 |
| **RACE** n (%) | | | | |
| WHITE | 155 (61) | 47 (59) | 19 (61) | 221 (60) |
| BLACK | 59 (23) | 16 (20) | 4 (13) | 79 (22) |
| ASIAN | 14 (5) | 10 (12) | 3 (10) | 27 (7) |
| OTHER | 27 (11) | 7 (9) | 5 (16) | 39 (11) |

*MEDIAN VALUES (RANGE)

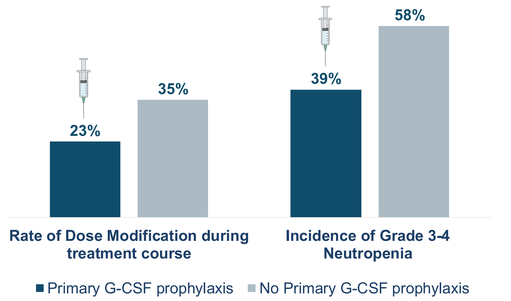
## RESULTS

### STARTING DOSE DISTRIBUTION AND DOSE REDUCTION RATES




- Among 366 patients, most initiated SG at 10 mg/kg (70%), with fewer starting at 7.5 mg/kg (22%) or 5 mg/kg (8%)
- Most common reason for dose-reduction was neutropenia (66%) followed by diarrhea (22%) and fatigue (17%). Only 3 patients discontinued treatment due to toxicity
- Median time to dose reduction **35 days** (range 7-1062 days)ß

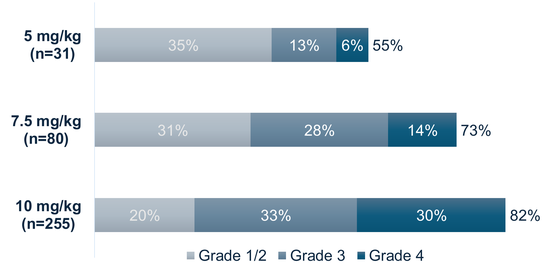
### CLINICAL OUTCOMES STRATIFIED BY PRIMARY G-CSF PROPHYLAXIS USE




### HOSPITAL ADMISSION RATES BY SG STARTING DOSE

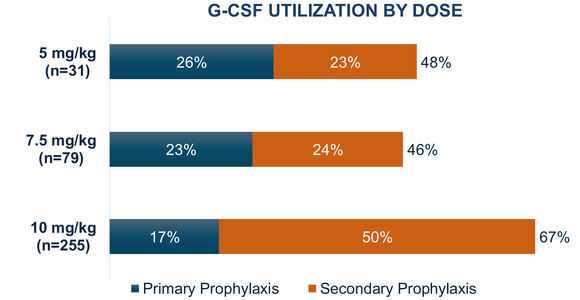
| | 10 mg/kg | 7.5 mg/kg | 5 mg/kg | Total |
|---|---|---|---|---|
| **HOSPITALIZATION DURING TREATMENT** n (%) | 83 (33) | 23 (29) | 8 (26) | 114 (31) |

### RATES OF NEUTROPENIA BY SG STARTING DOSE




- **Dose-dependent relationship** with severe neutropenia: 63% at 10 mg/kg, 42% at 7.5 mg/kg, 19% at 5 mg/kg
- 10 mg/kg confers 2.8-fold higher adjusted odds of grade 3-4 neutropenia compared to 5 mg/kg (OR 2.77, 95% CI 1.29-6.27, p=0.011)
- After IPW adjustment, Grade 3-4 **neutropenia rates did not differ** significantly by **race** (adjusted OR 1.41, 0.85-2.6, p=0.18), **age** (OR 1.00, 0.98-1.01), or **number of prior treatment lines** (OR 1.01, 0.93-1.13)

### G-CSF UTILIZATION BY DOSE




**Prophylactic G-CSF utilization:**

- Highest at lower starting doses
- Did not differ by age
- Reduced grade 3-4 events by 88% (OR 0.12, 95% CI 0.07-0.18, p<0.001) controlling for starting dose, prior treatment lines, or age
- Associated with numerically fewer hospitalizations

- After IPW adjustment, **no significant association** between **age** (OR 0.993 [0.98-1.006]), **starting dose** (OR 0.90 [0.55-1.56]), or **prior lines of therapy** (OR 0.952 [0.880-1.025]) and **hospitalization risk** was identified

## TAKEAWAY POINTS

- 70% of patients initiated at standard 10 mg/kg dose; 42% required dose reduction
- 10 mg/kg vs 5 mg/kg: **2.8-fold higher odds** of grade 3-4 neutropenia (OR 2.77, p=0.011)
- Prophylactic G-CSF: **88% risk reduction** in grade 3-4 neutropenia (OR 0.12, p<0.001)
- In this cohort, age was **not associated** with neutropenia risk or hospitalization after propensity score adjustment for starting dose, prophylactic G-CSF use, and prior treatment lines
- Neither starting dose nor prior treatment lines significantly affected hospitalization rates

## CLINICAL IMPLICATIONS

- Neutropenia remains the primary driver of dose modifications, and typically occurs early (median time 35 days)
- Prophylactic G-CSF and dose reduction are effective strategies for neutropenia prevention and were associated with a lower incidence of hospitalization
- These findings do not support empiric dose reduction based solely on advanced age

## FUTURE DIRECTIONS

- Evaluate impact of dose reduction on treatment efficacy to inform guidelines on primary G-CSF prophylaxis versus empiric dose reduction to maintain dose intensity
- Conduct larger prospective trials to identify patients at highest risk for severe neutropenia and establish evidence-based guidelines for primary G-CSF prophylaxis based on baseline risk factors