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# Calcitonin Prescribing Criteria for the Management of Hypercalcemia in a Community Hospital

Jessica Hernandez, Pharm.D.

Baptist Hospital of Miami, PGY-I Pharmacy Resident

# Disclosure Statement


- The following contributors have nothing to disclose regarding any financial or nonfinancial relationships with the products described, reviewed, or evaluated in this presentation
  - Jessica Hernandez, Pharm.D.
  - Radhan Gopalani, Pharm.D., BCPS
  - Heidi Clarke, Pharm.D., BCCCP
  - Joyce Lee, Pharm.D., BCCCP
  - Alyssa Donadio, Pharm.D., BCPS

# Objective

- I. Discuss the clinical impact of pharmacist interventions in implementing prescribing criteria for calcitonin at Baptist Hospital of Miami

# Hypercalcemia

Clinical condition defined as serum calcium levels exceeding the upper limit of normal (10.5 mg/dL).



## Classifications of hypercalcemia:

**Mild**= Corrected serum calcium < 12 mg/dL

**Moderate**= Corrected serum calcium 12-14 mg/dL

**Severe**= Corrected serum calcium >14 mg/dL

# Regulation of Calcium in the Plasma

- **Parathyroid Hormone (PTH)** → Increases serum calcium levels
  - Stimulates production of vitamin D within the kidney
  - Facilitates mobilization of calcium from bone
  - Maximizes tubular reabsorption of calcium within the kidney
- **1,25-dihydroxyvitamin D3 (Calcitriol)** → Increases serum calcium levels
  - Facilitates absorption of calcium from the small intestine
  - Enhances reflux of calcium out of bone
- **Calcitonin** → Reduces serum calcium levels
  - Secreted from thyroid gland in response to an increase in calcium blood concentrations
  - Promotes renal excretion of calcium

# Etiology of Hypercalcemia

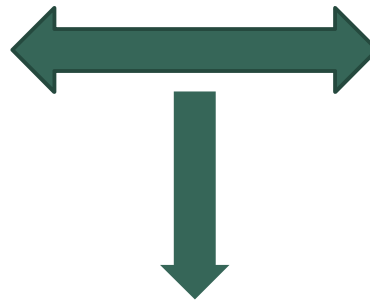
Primary hyperparathyroidism	Malignancy-associated hypercalcemia
Vitamin D intoxication	Medications <ul style="list-style-type: none"><li>• Thiazide diuretics</li><li>• Lithium</li><li>• Calcium containing antacids</li></ul>
Familial hypocalciuric hypercalcemia	Immobilization

# Hypercalcemia Treatment

★ **First-line therapy**

**Intravenous (IV)  
Hydration**

Recommended for  
mild, moderate & severe  
hypercalcemia



★ **First-line therapy**

**IV Bisphosphonates**

Recommended for  
moderate & severe  
hypercalcemia

**Calcitonin**

Reserved for  
moderate (symptomatic) &  
severe hypercalcemia



# Treatment

Therapy	Mode of Action	Dose	Onset of Action	Adverse Effects
IV fluids	<ul style="list-style-type: none"> <li>Increases glomerular filtration rate</li> <li>Enhances calcium excretion</li> </ul>	200-500 mL/hr or 2-4 L/day	Immediate	<ul style="list-style-type: none"> <li>Volume overload</li> <li>HF exacerbation</li> </ul>
Pamidronate	Inhibits osteoclast activity leading to decrease bone resorption	60-90 mg IV over 2-4 hours X 1 dose	<ul style="list-style-type: none"> <li>≤24 hours</li> <li>Maximum effect in ≤7 days</li> </ul>	<ul style="list-style-type: none"> <li>Nephrotoxicity</li> <li>Flu-like symptoms</li> </ul>
Zoledronic acid	Inhibits osteoclast activity leading to decrease bone resorption	4 mg IV over 15 minutes X 1 dose	<ul style="list-style-type: none"> <li>≤24 hours</li> <li>Maximum effect in ≤7 days</li> </ul>	<ul style="list-style-type: none"> <li>Nephrotoxicity</li> <li>Flu-like symptoms</li> </ul>
Calcitonin	<ul style="list-style-type: none"> <li>Inhibits osteoclast activity</li> <li>Enhances calcium excretion</li> </ul>	4-8 IU /kg SQ or IM every 12 hours	~2 hours	<ul style="list-style-type: none"> <li>Rebound effect</li> <li>Vomiting</li> <li>Cramps</li> <li>Flushing</li> </ul>

# Calcitonin (Miacalcin<sup>®</sup>)

- **FDA approved indications:**
  - Postmenopausal osteoporosis
  - Hypercalcemia
  - Paget's disease
- **Hypercalcemia Dosing:**
  - Dose: 4 units/kg IM/SQ every 12 hrs
  - May increase to 8 units/kg every 12 hrs if response is unsatisfactory
- **Concerns with overuse of calcitonin:**
  - Hypocalcemia
  - **Tachyphylaxis:** Hypocalcemic effect diminishes within 24 to 48 hours
  - **Price:** 400 units/2 mL (200 units/mL): **\$2,712.09**

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# Purpose

- 
- To assess the prescribing practices of calcitonin at Baptist Hospital of Miami (BHM) and to optimize the utilization of calcitonin in patients with hypercalcemia.
  - The intent of this project is to facilitate the implementation of a calcitonin prescribing criteria through pharmacist review and clinical recommendations at BHM

# Project design

- **Phase I:**

- Retrospective chart review of all patients who received calcitonin injections at Baptist Hospital of Miami (BHM) between October 1<sup>st</sup>, 2017-September 30<sup>th</sup>, 2019.

- **Phase II:**

- Prospective review post implementation of calcitonin prescribing criteria for the treatment of hypercalcemia.
- Resident will be on call to determine if initiation of calcitonin meets protocol criteria and make recommendations to the ordering physician as needed.

# Outcomes

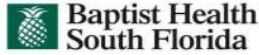
## Primary Outcome

Duration of calcitonin therapy (hrs)

## Secondary Outcomes

Number of pharmacy interventions

Percentage of patients treated with IV fluids and IV bisphosphonates



## Calcitonin (Miacalcin®) Prescribing Criteria for Hypercalcemia

### Introduction:

Calcitonin (Miacalcin®) is a synthetic hormone with a rapid onset of action and used intramuscularly (IM) or subcutaneously (SQ) as a second-line treatment in the management of hypercalcemia. Calcitonin lowers serum calcium levels by inhibiting bone resorption and enhancing calcium excretion in the urine. However, its use is reserved for the treatment of severe and symptomatic moderate hypercalcemia. Despite its rapid onset of action, the use of calcitonin in the management of hypercalcemia is limited due to its short duration of effect and the development of tolerance that results from downregulation of calcitonin receptors after 48 hours of treatment initiation.

### Etiology of hypercalcemia:

- Primary hyperparathyroidism
- Malignancy-associated hypercalcemia
- Vitamin D intoxication
- Medication induced hypercalcemia (eg. thiazide diuretics, lithium, calcium containing antacids)
- Immobilization

**Dose of calcitonin for the treatment of hypercalcemia:** 4 units/kg IM or SQ every 12 hours

### Calcitonin Prescribing Criteria:

1. Calcitonin should be reserved for **severe and symptomatic moderate hypercalcemia**
2. Pharmacist to review dose, dose increases, and duration of therapy consistent with guidelines (see table below for treatment guideline recommendations)
3. Pharmacist to monitor response of calcitonin daily by reviewing labs and limit use to **48 hours**.

### Calcitonin – Criteria for Use in Hypercalcemia

\* Use of calcitonin in hypercalcemia should be limited to **48 hours** due to diminish hypocalcemic effects beyond 48 hours

Calculate **Corrected Serum Calcium (CSC)** using the following formula:

**Serum calcium + 0.8 (4 – patient's albumin)**

<b>Severe hypercalcemia w/wo symptoms</b> (CSC ≥ 14 mg/dL)	<ul style="list-style-type: none"> <li>• <b>IV normal saline:</b> 200-500 mL/h or 2-4 L/d</li> <li>• <b>Pamidronate:</b> 60-90 mg IV over 2-4 hours as a single dose (allow at least 7 days before retreatment)</li> <li>• <b>Calcitonin:</b> 4 units/kg IM or SQ every 12 hrs</li> </ul>	
<b>Moderate symptomatic hypercalcemia</b> (CSC 12-13.9 mg/dL)	<ul style="list-style-type: none"> <li>• <b>IV normal saline:</b> 200-500 mL/h or 2-4 L/d</li> <li>• <b>Pamidronate:</b> 60-90 mg IV over 2-4 hours as a single dose (allow at least 7 days before retreatment)</li> <li>• <b>Calcitonin:</b> 4 units/kg IM or SQ every 12 hrs</li> </ul>	<b>Symptoms of hypercalcemia:</b> <ul style="list-style-type: none"> <li>• Nausea/Vomiting</li> <li>• Constipation</li> <li>• Lethargy and fatigue</li> <li>• Muscle weakness</li> <li>• Polyuria</li> <li>• Nephrolithiasis</li> <li>• Acute renal insufficiency</li> <li>• Shortened QT interval</li> </ul>
<b>Moderate asymptomatic hypercalcemia</b> (CSC 12-13.9 mg/dL)	<ul style="list-style-type: none"> <li>• <b>IV normal saline:</b> 200-500 mL/h or 2-4 L/d</li> <li>• <b>Pamidronate:</b> 60-90 mg IV over 2-4 hours as a single dose (allow at least 7 days before retreatment)</li> </ul> <p>*Calcitonin is not to be used in this setting</p>	
<b>Mild hypercalcemia</b> (CSC ≤ 11.9 mg/dL)	<ul style="list-style-type: none"> <li>• Do not require immediate treatment</li> <li>• <b>IV normal saline:</b> 200-500 mL/h or 2-4 L/d</li> </ul> <p>*Calcitonin is not to be used in this setting</p>	

## Calcitonin (Miacalcin®) Optimization Project

Principal Investigator (PI): Jessica Hernandez, PharmD, PGY-1 Pharmacy Resident

### Rationale:

Calcitonin should be reserved for **severe and symptomatic moderate hypercalcemia** (please see Calcitonin Prescribing Criteria attachment)

### Purpose:

To optimize the utilization of calcitonin in patients with hypercalcemia and reduce cost

- ❖ Prospective chart review will be conducted for every calcitonin order to determine if it meets treatment guideline recommendations
- ❖ Goal is to intervene and review chart prior to verification of calcitonin

### Pharmacist's role:

- ❖ **Prior to verifying any order for calcitonin, please contact Jessica Hernandez, PGY-1 Resident**
- ❖ **Time frame:** January 6<sup>th</sup> – April 24<sup>th</sup> 2020
- ❖ **On Call from 7am – 7pm (including weekends)**
  - ASCOM: 54217
  - Cell: 561-685-2081
- ❖ **For any orders outside of time frame:**
  - List name, FIN, and room number on attached sheet and leave in designated basket in resident's office.
  - Prior to verifying order, calculate for corrected serum calcium (CSC) for hypoalbuminemia in order to see if calcitonin is warranted.

**CSC = Serum calcium + 0.8 (4 – patient's albumin)**

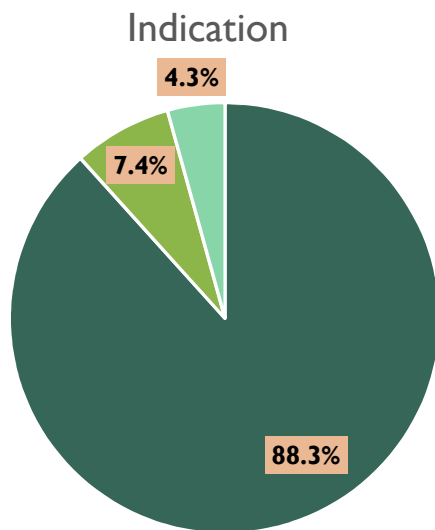
**Thank you!**

# Baseline Demographics

	Phase I (N=94)	Phase II (N=16)
Mean age, years	69	68
Gender – male, n (%)	53 (56.4)	4 (25)
Mild Hypercalcemia, n (%)	13 (13.8)	7 (43.8)
Moderate Asymptomatic Hypercalcemia, n (%)	9 (9.6)	2 (12.5)
Moderate symptomatic Hypercalcemia, n (%)	31 (33)	4 (25)
Severe Hypercalcemia, n (%)	41 (43.6)	3 (18.8)

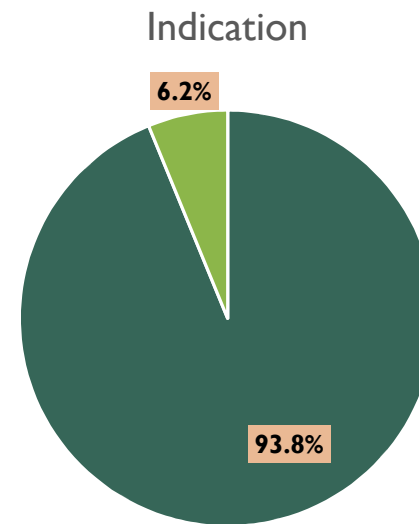
# Demographics

## ■ Phase I:



■ Hypercalcemia of Malignancy ■ Primary Hyperparathyroidism ■ Other

## ■ Phase II:



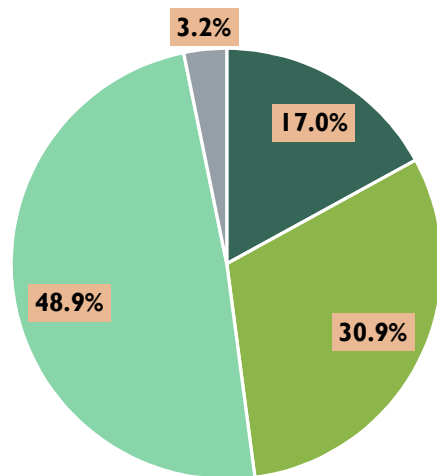
■ Hypercalcemia of Malignancy ■ Primary Hyperparathyroidism



# Demographics

## ■ Phase I:

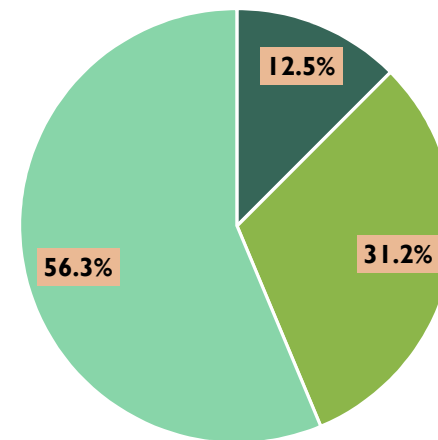
Ordering Provider Specialty



■ Internal Medicine ■ Nephrology ■ Oncology ■ Other

## ■ Phase II:

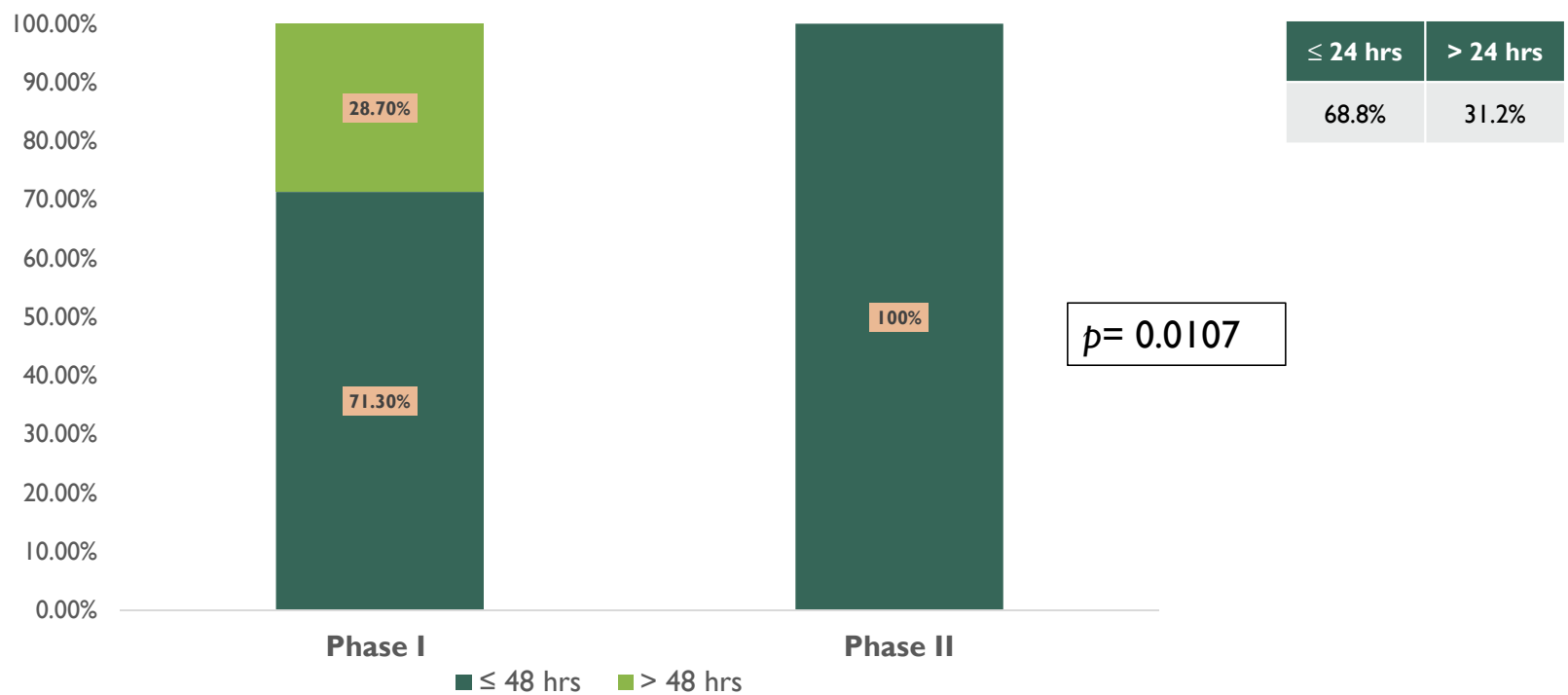
Ordering Provider Specialty



■ Internal Medicine ■ Nephrology ■ Oncology

# Results: Primary Outcome

## Duration of Calcitonin Therapy



# Results: Secondary Outcomes

- Number of pharmacy interventions = 16
  - 75% acceptance rate
- Usage of first-line therapy:

	Phase I (N=94)	Phase II (N=16)	p-value
IV Fluids – n (%)	76 (81)	16 (100)	p= 0.0689
IV Bisphosphonates – n (%)	83 (88)	16 (100)	p= 0.3613

# Pharmacist Interventions

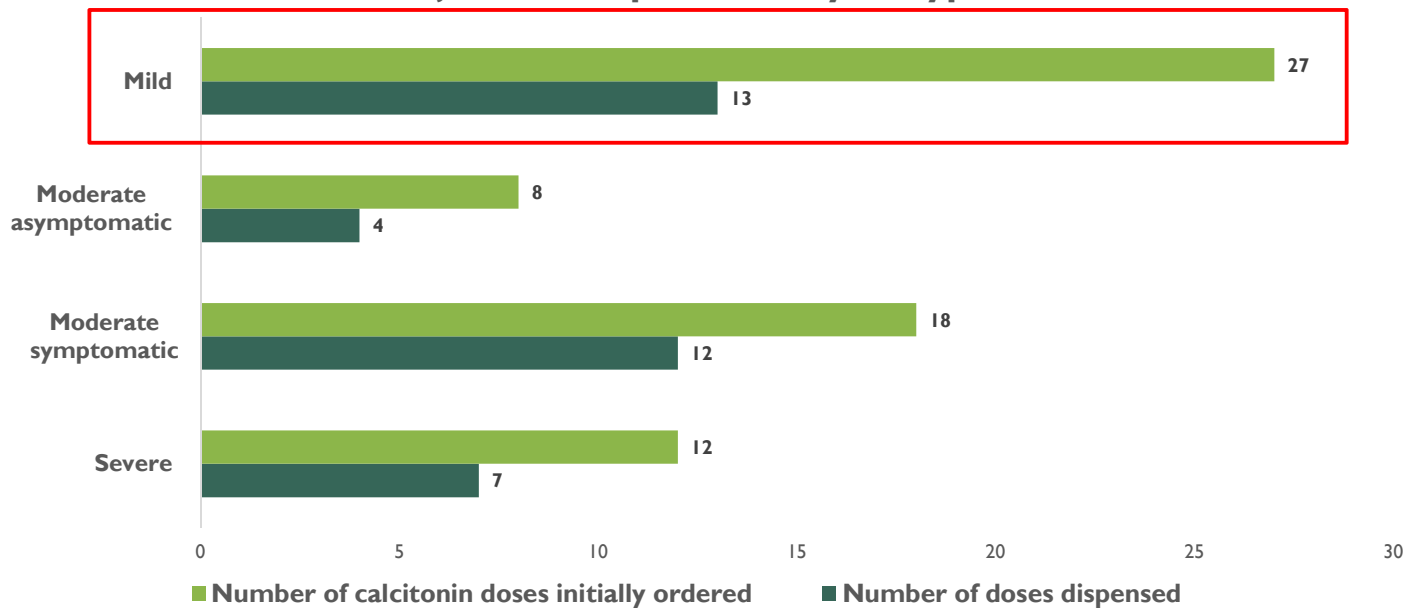
Severity of Hypercalcemia	Discontinuation of Calcitonin	Shorten Duration of Therapy	Declined
Mild (n=7)	2	3	2
Moderate Asymptomatic (n=2)	0	2	0
Moderate Symptomatic (n=4)	N/A	2	2
Severe (n=3)	N/A	3	0

$$\frac{12 \text{ interventions accepted}}{16 \text{ total interventions}} = 75\% \text{ acceptance rate}$$

# Results: Secondary Outcomes

## ■ Phase II:

Total dose adjustments per severity of hypercalcemia



### Reasons for dispensing calcitonin for mild hypercalcemia

Presence of symptoms

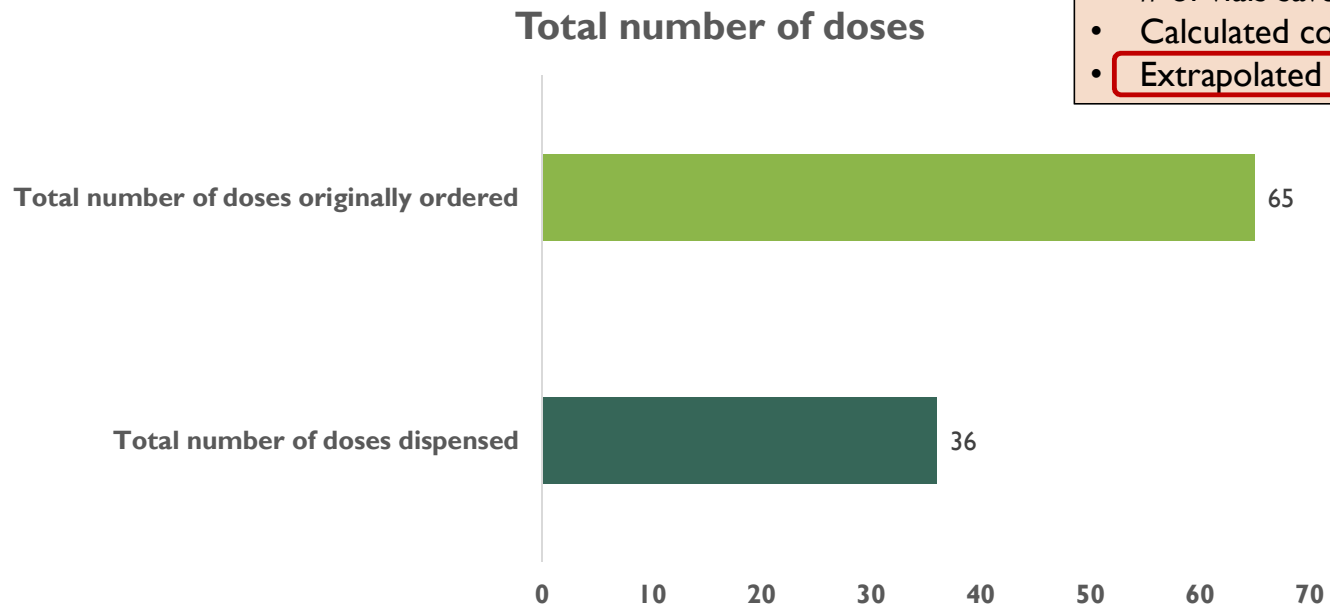
Failure to first-line therapy

Delayed notification to the PI of order

# Results: Secondary Outcomes

## ■ Phase II:

- # of doses reduced by 45%
- # of vials saved: 18
- Calculated cost savings ~\$48,000 cost savings
- **Extrapolated BHM cost savings ~ \$158,000/year**



# Discussion

- **Limitations:**

- Low volume of calcitonin orders due to short duration of phase II
- Inability to accurately assess for presence of symptoms for hypercalcemia
  - e.g., fatigue due to hypercalcemia vs. underlying disease
  - Lack of documentation of symptoms

- **Opportunities:**

- Educate pharmacists on optimal calcitonin use and monitoring
- Establish prescribing criteria to facilitate utilization of calcitonin across Baptist Health-System
- Develop electronic order-sets for the treatment of hypercalcemia based on severity level

# Conclusion

- Implementation of a calcitonin prescribing criteria through active pharmacist review and recommendations can facilitate the optimization of calcitonin use in patients with hypercalcemia at BHM and potentially lead to cost savings.



# Post-Assessment

- Which of the following classifications of hypercalcemia is calcitonin recommended for?
  - A. Moderate symptomatic hypercalcemia
  - B. Severe hypercalcemia
  - C. Asymptomatic moderate hypercalcemia
  - D. A & B

# References

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