

# UPDATES IN CARDIAC PHARMACOTHERAPY

Paige Skelton, Pharm.D.

Abbott Northwestern Hospital

Tuesday February 27<sup>th</sup>, 2018



## DISCLOSURE

- I have no financial interest or affiliation with the manufacturer of any marketed product discussed herein.



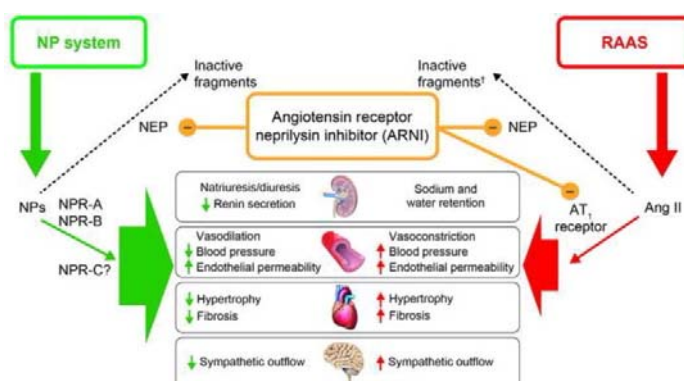
## OBJECTIVES

- To recognize and understand new cardiac medications and their use within the cardiac patient population
  - Sacubitril/valsartan (Entresto)
  - Ivabradine (Corlanor)
  - Idarucizumab (Praxbind)
  - Cangrelor (Kengreal)
  - Angiotensin II (Giapreza)



## SACUBITRIL/VALSARTAN (ENTRESTO)

- **Mechanism of action:**
  - Sacubitril – neprilysin inhibitor
  - Valsartan – angiotensin receptor blocker (ARB)
- **Drug class:**
  - Angiotensin-receptor neprilysin inhibitor (ARNI)
- **FDA approved indication:**
  - Chronic heart failure, class II to IV



## SACUBITRIL/VALSARTAN (ENTRESTO)

### ▪ Dosing:

- Entresto 49/51 mg twice daily
  - Previously on a moderate to high dose of an ACE-I or ARB
- Entresto 24/26 mg twice daily
  - Previously on a low dose of an ACE-I or ARB
  - No prior ACE-I or ARB
  - eGFR < 30 mL/min
- Titrate every 2-4 weeks to goal dose of 97/103 mg twice daily



### ▪ Administration:

- With or without food
- Do **NOT** crush or chew tablets
- Do **NOT** give within 36 hours of an ACE-I

Entresto® [prescribing information]. Novartis. Nov 2017.



## SACUBITRIL/VALSARTAN (ENTRESTO)

### ▪ Adverse effects:

- Hypotension
- Increased SCr
- Hyperkalemia
- Angioedema

### ▪ Contraindications:

- Concomitant ACE-I or aliskiren use
- Angioedema with prior ACE-I or ARB

### ▪ Monitoring:

- Blood pressure
- Renal function (SCr)
- Serum potassium



Entresto® [prescribing information]. Novartis. Nov 2017.



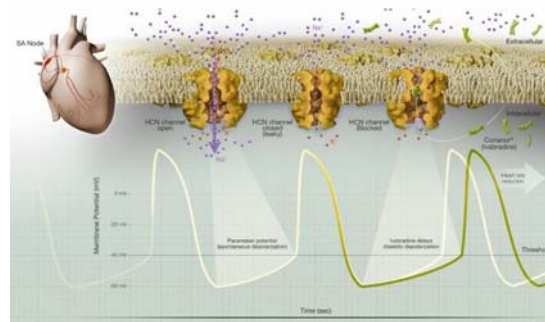
## IVABRADINE (CORLANOR)

- **Mechanism of action:**

- Reduces pacemaker activity at the cardiac sinus node by selectively inhibiting the I(f)-current

- **FDA approved indication:**

- Chronic heart failure
  - LVEF  $\leq 35\%$
  - NSR with resting HR  $\geq 70$  bpm
  - On maximally tolerated doses of beta-blockers OR have a contraindication to the use of beta-blockers



Corlanor® [prescribing information]. Amgen. Jan 2017.



## IVABRADINE (CORLANOR)

- **Dosing:**

- Starting dose: Corlanor 2.5 to 5 mg twice daily
- Max dose: 7.5 mg twice daily
- Titrate to resting HR goal of 50 – 60 bpm

- **Administration:**

- Take with food
- Do NOT crush or chew tablets



Corlanor® [prescribing information]. Amgen. Jan 2017.



## IVABRADINE (CORLANOR)

### Adverse effects:

- Bradycardia
- Hypertension
- Atrial fibrillation
- Phosphenes

### Monitoring:

- Heart rate
- Blood pressure
- Cardiac rhythm

### Contraindications:

- ADHF
- Blood pressure < 90/50 mmHg
- Heart rate < 60 bpm prior to initiation
- Pacemaker dependence
- Sick sinus syndrome
- SA node block or third degree AV block
- Severe hepatic impairment
- Concomitant use with strong CYP3A4 inhibitors

Corlanor® [prescribing information]. Amgen. Jan 2017.



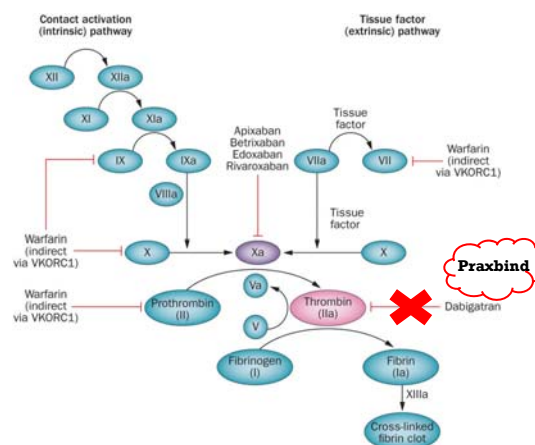
## IDARUCIZUMAB (PRAXBIND)

### Mechanism of action:

- Humanized monoclonal antibody
- Neutralizes the anticoagulant effect of dabigatran (Pradaxa)

### FDA approved indication:

- Reversal of dabigatran for emergency surgery/urgent procedures or in life-threatening or uncontrolled bleeding



Sabir I, et al. *Nat Rev Cardiol*. 2014. 11,290-303.  
Praxbind® [prescribing information]. Boehringer Ingelheim Inc. Oct 2015.



## IDARUCIZUMAB (PRAXBIND)

### ■ Dosing:

- 5 g, provided as two separate vials each containing 2.5 g/50 mL
- Limited efficacy and safety on repeat dosing

### ■ Administration:

- Two consecutive infusions OR bolus injection by injecting both vials consecutively one after another via syringe
- Infuse over 5 minutes with each dose separated no more than 15 minutes apart
- Do NOT shake or tube



Praxbind® [prescribing information]. Boehringer Ingelheim Inc. Oct 2015.



## IDARUCIZUMAB (PRAXBIND)

### ■ Adverse effects:

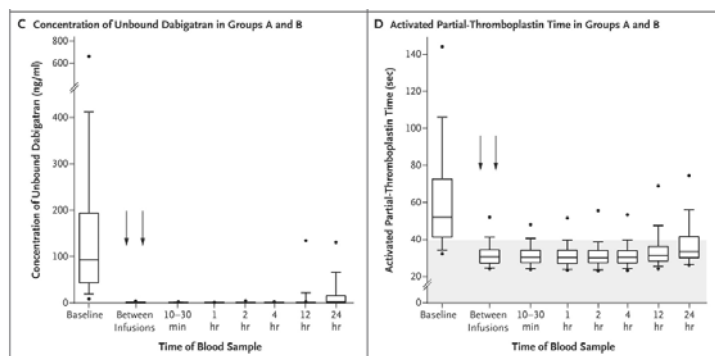
- Thromboembolic disorder
- Hypokalemia
- Delirium
- Fever

### ■ Monitoring:

- Reversal of anticoagulant effects

### ■ Contraindications:

- None



*N Engl J Med* 2017;377:341-441.  
Praxbind® [prescribing information]. Boehringer Ingelheim Inc. Oct 2015.



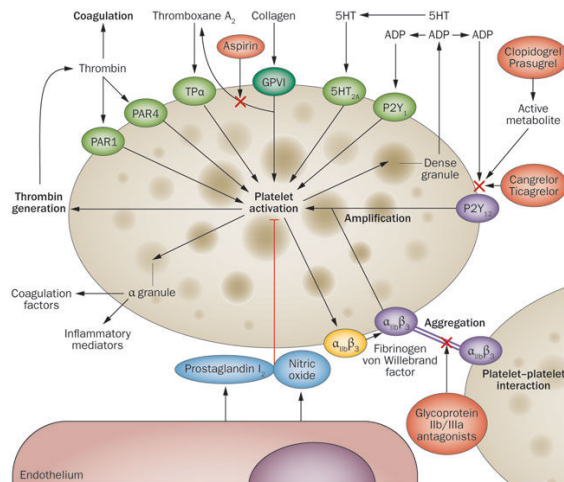
## CANGRELOR (KENGREAL)

### ▪ Mechanism of action:

- Selective, reversible P2Y<sub>12</sub> platelet inhibitor
- Blocks ADP-induced activation and aggregation of platelets

### ▪ FDA approved indication:

- Adjunct to PCI in patients who did not receive an oral P2Y<sub>12</sub> inhibitor or a GP 11b/IIIa inhibitor



*Nat Rev Cardiol.* 2013. 10, 302-304.  
Kengreal® [prescribing information]. The Medicines Company. June 2015.

## CANGRELOR (KENGREAL)

### ▪ PCI Dosing:

- 30 mcg/kg IV bolus followed by 4 mcg/kg/min IV infusion
- Initiate bolus infusion prior to PCI
- Maintenance infusion should be continued for at least 2 hours or for the duration of the PCI

### ▪ Bridging Dosing (off-label):

- 0.75 mcg/kg/min with no bolus
- Discontinue thienopyridine up to 7 days prior to surgery
- Discontinue cangrelor 1-6 hours prior to incision

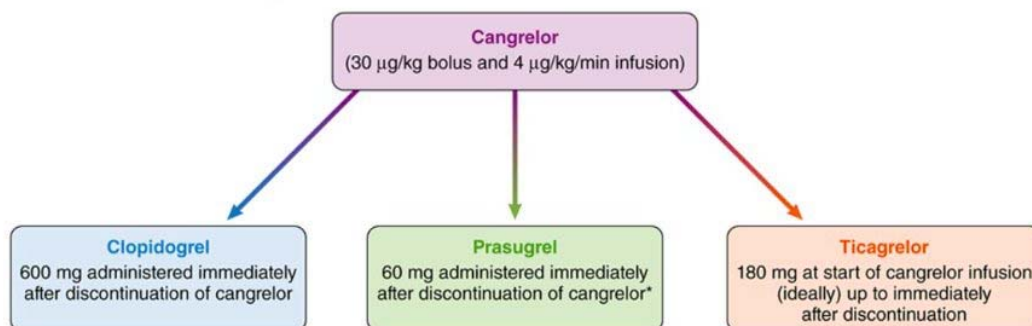
### ▪ Administration:

- Must be diluted prior to use
- Administer via a dedicated IV line

Kengreal® [prescribing information]. The Medicines Company. June 2015.

# CANGRELOR (KENGREAL)

## B Transition from IV to oral P2Y<sub>12</sub> inhibitors



Angiolillo DJ et al. *Circulation*. 2017;136:00-00.



# CANGRELOR (KENGREAL)

- **Adverse effects:**
  - Bleeding
  - Hypersensitivity
  - Decreased renal function
  - Dyspnea
- **Monitoring:**
  - Signs of bleeding
- **Contraindications:**
  - Significant active bleeding



Kengreal® [prescribing information]. The Medicines Company. June 2015.





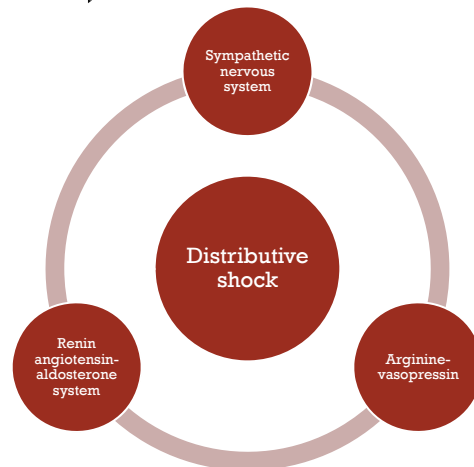
## ANGIOTENSIN II (GIAPREZA)

- **Mechanism of action:**

- Synthetic human angiotensin II
- Increases blood pressure by vasoconstriction and increased aldosterone release

- **FDA approved indication:**

- Increase blood pressure in adults with septic or distributive shock



Giapreza® [prescribing information]. La Jolla Pharmaceutical Co. December 2017.



## ANGIOTENSIN II (GIAPREZA)

- **Dosing:**

- Starting dose: 20 ng/kg/min
- May increase by 15 ng/kg/min every 5 minutes
- Do not exceed 80 ng/kg/min within first 3 hours

- **Administration:**

- Must be diluted prior to use
- Continuous infusion via a central line



Giapreza® [prescribing information]. La Jolla Pharmaceutical Co. December 2017.



## ANGIOTENSIN II (GIAPREZA)

- **Adverse effects:**

- Hypertension
- Thromboembolic events
- Thrombocytopenia
- Tachycardia
- Delirium
- Hyperglycemia

- **Monitoring:**

- Blood pressure
- VTE events

- **Contraindications:**

- None

Giapreza® [prescribing information]. La Jolla Pharmaceutical Co. December 2017.



## SUMMARY

- Sacubitril/valsartan (Entresto) is an ARNi approved for chronic heart failure
- Ivabradine (Corlanor) is a funny current inhibitor approved for chronic heart failure
- Idarucizumab (Praxbind) is a reversal agent for dabigatran (Pradaxa)
- Cangrelor (Kengreal) is a P2Y<sub>12</sub> platelet inhibitor approved as an adjunct to PCI
- Giapreza is a synthetic human angiotensin II approved for septic and distributive shock



## REFERENCES

- 1) Entresto (sacubitril/valsartan) [prescribing information]. East Hanover, NJ: Novartis; November 2017.
- 2) Corlanor (ivabradine) [prescribing information]. Thousand Oaks, CA: Amgen Inc; January 2017.
- 3) Praxbind (idarucizumab) [prescribing information]. Ridgefield, CT: Boehringer Ingelheim Pharmaceuticals, Inc; October 2015.
- 4) Kengreal (cangrelor) [prescribing information]. Parsippany, NJ: The Medicines Company; June 2015.
- 5) Giapreza [prescribing information]. San Diego, CA: La Jolla Pharmaceutical Company; December 2017.



## CONTACT INFORMATION

- Paige Skelton, Pharm.D.  
PGY2 Cardiology Pharmacy Resident  
Abbott Northwestern Hospital
- Email: [paige.skelton@allina.com](mailto:paige.skelton@allina.com)

