New Drugs and Their Appropriate Use

Joseph Ming Wah Li, MD
Director, Hospital Medicine Program
Associate Chief, Division of General Medicine
Beth Israel Deaconess Medical Center
Associate Professor of Medicine
Harvard Medical School
Boston, MA

Disclosure of relevant relationships
• ACP Education & Publication Committee member
• Elsevier publisher: author & editor honoraria
• Employment: Harvard Medical Faculty Physicians at Beth Israel Deaconess Medical Center
• John Wiley & Sons publisher: author honoraria
• MA DPH stroke advisory committee member
• QuantiaMD consultant
• Society of Hospital Medicine board member
• Test writing committee member:
  – ABIM hospital medicine maintenance of cert. exam
  – NBME USMLE Step 3 exam

Discussion topics
• FDA approved drugs Jan 2010 - now
• New drugs most relevant to hospitalists
• Clinical case scenarios
• What is likely coming next year?
• Disclaimer…
FDA Drug Approval Process

FDA Drug Approvals

<table>
<thead>
<tr>
<th>Yr</th>
<th># drugs FDA approved</th>
</tr>
</thead>
<tbody>
<tr>
<td>2010</td>
<td>21</td>
</tr>
<tr>
<td>2009</td>
<td>25</td>
</tr>
<tr>
<td>2008</td>
<td>24</td>
</tr>
<tr>
<td>2007</td>
<td>18</td>
</tr>
</tbody>
</table>

FDA Approvals 2010

- **CV**
  - Aliskiren + amlodipine
  - Olmesartan + amlodipine

- **Endocrine**
  - Denosumab
    (Prolia) For pts w/ osteoporosis at risk for fractures
    (Xgeva) For prevention of skeletal related events in pts w/ bone mets from solid tumors
  - Liraglutide: for type 2 DM
FDA Approvals 2010

- **GI**
  - Ondansetron soluble film

- **Hematology**
  - Velaglucerase: for Type 1 Gaucher dz
FDA Approvals 2010

• Oncology
  - Eribulin: for late stage metastatic breast cancer after prev therapies
  - Cabazitaxel: for hormone refractory prostate CA
  - Sipuleucel-T: pt specific vaccine for hormone refractory prostate CA

Sipileucel - T

FDA Approvals 2010

• Immunology / ID
  – Aztreonam for inhalation
  – 2nd Meningococcal conjugate vaccine
  – Tesamorelin: for HIV pts w/ lipodystrophy
FDA Approvals 2010

- Rheumatology
  - Naproxen + esomeprazole
  - Tocilizumab: for rheumatoid arthritis
  - Pegloticase: for chronic gout

Pegloticase: Gout Treatment
Pegloticase

- Recommended dose: 8mg IV over 2 hours every 2 wks
- To minimize risk of anaphylaxis & infusion rxns, pre-med w/ antihistamines & steroids; monitor pts for appropriate period of time after drug given
- Stop drug in event of severe infusion rxn; risk higher in pts who have lost therapeutic response
- Development of anti-pegloticase antibodies assoc w/ loss of treatment response.

FDA Approvals 2010

- Nephrology / urology
  - Carglumic acid: for hyperammonemia due to N-acetylglutamate synthase deficiency
  - Dutasteride + tamsulosin: for BPH
- Neurology
  - Dalfampridine: to improve walking in pts w/ MS
  - Fingolimod: treat relapsing MS

Fingolimod: FREEDOMS Trial
Fingolimod: TRANSFORMS Trial

FDA Approvals 2010

- Pulmonary
  - Mometason + Formoterol: treat asthma

- Pain
  - Hydromorphone extended release
  - Naltrexone extended release injectable suspension

New drugs – most pertinent to hospitalists

<table>
<thead>
<tr>
<th>Drug</th>
<th>Indication</th>
<th>Class</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ceftaroline</td>
<td>CAP, ABSSSI</td>
<td>Antimicrobial</td>
</tr>
<tr>
<td>Pneumococcal conjugate vaccine</td>
<td>Prevent invasive disease</td>
<td>Vaccine</td>
</tr>
<tr>
<td>Dabigatran</td>
<td>Reduce CVA risk due to afib</td>
<td>Anticoagulant</td>
</tr>
</tbody>
</table>
**Patient presentation**

- 75 yo female smoker who lives at home with family. She has a history of DM 2, Afib & chronic systolic HF. She presents to the hospital c/o fever, sob & cough productive of rust-colored sputum. No history of hospitalization. Meds: metformin, lisinopril & coumadin

  T38.5 (101F)  BP 143/77  HR 100  RR 20 93%RA
  
  Diaphoretic, crackles at L base;
  
  CXR=L2L infiltrate
  
  Labs normal except for INR 1.7, BUN 25 mg/DL, BS 252 mg/DL

---

**Clinical question**

- The nurse asks which drug you would like to prescribe to treat this patient’s pneumonia?
  
  A) Ceftriaxone and azithromycin
  
  B) Levofloxacin
  
  C) Ceftriaxone
  
  D) Vancomycin
  
  E) Ceftaroline

---

**Pneumonia: definitions**

- CAP: occurs as outpatient or < 48 hrs after hospital admission
  
  HCAP: occurs in non-hospitalized patient with extensive healthcare contact
  
  HAP: occurs >48 hrs after hosp admission
  
  VAP: type of HAP that arises 48-72 hrs after endotracheal intubation
Healthcare assoc pneumonia

- Hospitalization for 2 or more days within past 90 days
- IV antibiotics, IV chemotherapy or wound care within past 30 days of infection
- Residence in skilled nursing facility or long-term care facility
- Attendance at hospital or hemodialysis clinic within prior 30 days

Pneumonia Patient Outcomes Research Team (PORT) Study


Pneumonia Patient Outcomes Research Team (PORT) Study

- Analyzed database w/ 14K adult inpts w/ CAP to create prediction rule that stratifies pts into 5 classes w/ respect to risk of death within 30 days.
- Prediction rule assigns pts to a class based on pt variables
- Prediction validated using database w/ 38K inpts w/ CAP.
**Patient presentation**

- 75 yo female smoker who lives at home with family. She has a history of DM 2, Afib & chronic systolic HF. She presents to the hospital c/o fever, sob & cough productive of rust-colored sputum. No history of hospitalization. Meds: metformin, lisinopril & coumadin

T38.5 (101F) BP 143/77 HR 100 RR20 93%RA
Diaphoretic, crackles at L base;
CXR=Lll infiltrate
Labs normal except for INR 1.7, BUN 25 mg/DL, BS 252 mg/DL
PSI 85 (Class 3)
CAP Therapy: CURB-65

Modified BTS criteria:
- Confusion
- Urea > 7 mmol/L (20mg/DL)
- Respiratory rate > 30/min
- BP: systolic BP < 90 mm Hg or
  diastolic BP < 60 mm Hg
- 65 years and older

30 day mortality with modified BTS criteria:

0 factors: 0.7%
1 factor: 2.1%
2 factors: 9.2%
3 factors: 14.5%
4 factors: 40%
5 factors: 50%

- One point for each characteristic
- Score 3 or greater: admit to ICU
- Score = 2: admit to hospital general ward
- Score 0 or 1: outpatient therapy
- ?easier to administer than PSI Score?
Patient presentation

- 75 yo female smoker w/ DM 2, Afib, chronic systolic HF presents to the hospital c/o fever, sob & cough productive of rust-colored sputum.

T38.5 (101F) BP 143/77 HR 100 RR20 93%RA
Diaphoretic, crackles at L base;
CXR=LLL infiltrate
Labs normal except for BUN 25 mg/DL & BS 252 mg/DL

PSI = 85 (Class 3)   CURB-65 = 2

CAP: IDSA/ATS Guideline

- Inpatients (non-ICU)
  - respiratory fluoroquinolone
  - or
  - beta lactam (e.g. ceftriaxone, high dose amoxicillin, etc) + macrolide (level 1 data)

Ceftaroline: FOCUS 1 & 2

Question: Is ceftaroline non-inferior to ceftriaxone in CAP?
Design: 2 randomized, double-blind multicenter trials

File TM, et al. CID 2010;51(12):1385-1405
Focus 1 & 2

• Inclusion:
  PSI class 3 or 4; 18 yrs or older
• Exclusion:
  Outpts and pts admitted to ICU
  HCAP
  Empyema
  MRSA risk factors
  Suspected atypical pathogen
  Severe renal or liver dz

Focus 1 & 2: Results

• Focus 1: Clinical cure rates in CE pop
  Ceftaroline 86.6%
  Ceftriaxone 78.2%
  (diff 8.4%; 95% CI, 1.4%-15.4%)
• Focus 2: Clinical cure rates in CE pop
  Ceftaroline 82.1%
  Ceftriaxone 77.2%
  (diff 4.9%; 95% CI, -2.5% to 12.5%)

Ceftaroline: FDA Indications

• Treatment of following infections caused by susceptible bacteria:
  - Acute bacterial skin & skin structure infection (5-14 d)
  - Community acquired pneumonia (5-7 d)
• Dosing:
  600mg q 12 IV infusion over 1 hr in adults
  18 yo or older
Ceftaroline: Dosing adjustments

<table>
<thead>
<tr>
<th>Est CrCL (ml/min)</th>
<th>Dosing</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt; 50</td>
<td>No dose adjustment</td>
</tr>
<tr>
<td>&gt; 30 to \leq 50</td>
<td>400mg IV q 12 hrs</td>
</tr>
<tr>
<td>\geq 15 to \leq 30</td>
<td>300mg IV q 12 hrs</td>
</tr>
<tr>
<td>ESRD (&lt;15), HD</td>
<td>200mg IV q 12</td>
</tr>
<tr>
<td>- give after HD on HD days</td>
<td>All infusions over 1 hr</td>
</tr>
</tbody>
</table>

Ceftaroline: precautions

- Direct Coombs’ test seroconversion has been reported. If anemia develops during or after therapy, perform workup for drug-induced hemolytic anemia & consider stopping ceftaroline.

Back to our patient…

- 75 yo female smoker who lives at home with family. She has a history of DM 2, Afib & chronic systolic HF. She presents to the hospital c/o fever, sob & cough productive of rust-colored sputum. No history of hospitalization. Meds: metformin, lisinopril & coumadin

  T38.5 (101F) BP 143/77 HR 126 RR 20 93%RA
  Diaphoretic, crackles at L base;
  CXR=Lll infiltrate
  Labs normal except for INR 1.7, BUN 25 mg/DL, BS 252 mg/DL
Back to our clinical question

- Which of the following should you prescribe to treat this patient’s pneumonia?
  A) Ceftriaxone and azithromycin
  B) Levofloxacin
  C) Ceftriaxone
  D) Vancomycin
  E) Ceftaroline

Next Clinical Question

- The pharmacist calls & asks you to clarify which pneumococcal vaccine you want to give to this patient. How do you respond?
  A) 14-valent polysaccharide
  B) 23-valent polysaccharide
  C) 7-valent conjugate
  D) 13-valent conjugate
  E) I have no clue – just give what we normally give and don’t bother me…
Pneumococcal invasive disease

- Invasive dz: presence of bacteria in body fluids which are normally sterile: blood, CSF, pleural fluid, ascites or synovial fluid.
- Invasive dz from *S. pneumoniae* is major cause of illness in US w/ est 43,500 cases & 5,000 deaths in 2009
- Invasive pneumococcal dz has mean mortality of 10% with >30% in high risk groups (nursing home residents >65 yo).

Pneumococcal invasive disease

risk factors

- Immunodeficiency (congenital or acquired)
- Chronic heart, lung (including asthma), renal or liver disease
- DM
- Asplenia (congenital or surgical)
- Heavy alcohol use
- Smoking

### Table: Underlying medical conditions or other indications for administration of 23-valent pneumococcal polysaccharide vaccine (PPSV23) among adults aged 19–64 years, by risk group — Advisory Committee on Immunization Practices (ACIP) 2010

<table>
<thead>
<tr>
<th>Risk group</th>
<th>Underlying medical condition or other indication</th>
</tr>
</thead>
<tbody>
<tr>
<td>Immunocompromised person</td>
<td>Chronic heart disease, including hypertrophic*</td>
</tr>
<tr>
<td></td>
<td>Chronic lung disease*</td>
</tr>
<tr>
<td></td>
<td>Diabetes mellitus</td>
</tr>
<tr>
<td></td>
<td>Hematopoietic stem cell transplant</td>
</tr>
<tr>
<td></td>
<td>Chronic liver disease, including cirrhosis</td>
</tr>
<tr>
<td></td>
<td>Cigarette smoking</td>
</tr>
<tr>
<td>Persons with functional or anatomic asplenia*</td>
<td>Severe combined immunodeficiency*</td>
</tr>
<tr>
<td></td>
<td>Congenital or acquired immunodeficiency*</td>
</tr>
<tr>
<td></td>
<td>HIV infection</td>
</tr>
<tr>
<td></td>
<td>Chronic renal failure</td>
</tr>
<tr>
<td></td>
<td>Neutropenia</td>
</tr>
<tr>
<td></td>
<td>Immunosuppressive therapy</td>
</tr>
<tr>
<td></td>
<td>Radiation therapy</td>
</tr>
<tr>
<td></td>
<td>Goodpasture syndrome</td>
</tr>
<tr>
<td></td>
<td>Guillain–Barré syndrome</td>
</tr>
<tr>
<td></td>
<td>Severe neutropenia</td>
</tr>
<tr>
<td></td>
<td>Disease requiring treatment with immunosuppressive drugs, including long-term systemic corticosteroids or radiation therapy</td>
</tr>
<tr>
<td></td>
<td>Solid organ transplantation</td>
</tr>
<tr>
<td></td>
<td>会计科目的</td>
</tr>
</tbody>
</table>

*Clinical judgment may be necessary.
### ACIP PPSV23 rec for adults

- PPSV23 should be administered to adults aged 19-64 years with chronic or immune-suppressing medical conditions, including those who have asthma.
- Adults aged 19-64 years who smoke cigarettes should receive PPSV23 and smoking cessation guidance.
- Routine PPSV23 use is no longer recommended for Alaska Natives or American Indians aged >65 years unless they have medical indications for PPSV23. However, in certain situations, public health authorities may recommend PPSV23 for Alaska Natives and American Indians aged 50-64 years who are living in areas where the risk for invasive pneumococcal disease is increased.
- All persons should be vaccinated with PPSV23 at age 65 years. Those who received PPSV23 before age 65 years for any indication should receive another dose of the vaccine at age 65 years or later if at least 5 years have passed since their previous dose. Those who receive PPSV23 at age 65 or older age 65 years should receive only a single dose.
- ACIP does not recommend routine revaccination for most persons for whom PPSV23 is indicated. A second dose of PPSV23 is recommended 5 years after the first dose for persons aged 19-65 years with functional or anatomic asplenia and for persons with immunosuppressing conditions. ACIP does not recommend multiple revaccinations because of uncertainty regarding clinical benefit and safety.

### Pneumococcal vaccines

- 1977 14-valent polysaccharide vaccine
- 1983 23-valent polysaccharide vaccine (Pneumovax)
- 2000 7-valent conjugate vaccine (PCV7)
- 2010 13-valent conjugate vaccine (PCV13)

### Indirect effects of routine infant vaccination w/ PCV7

- Reduced incidence of invasive pneumococcal disease (IPD) among unvaccinated persons of all ages
- Reduction IPD rates from 1998 to 2008:
  - 18-49 yo: 34%
  - 50-64 yo: 14%
  - 65 yo and older: 37%
- Measured indirect effects on non-invasive disease less clear
Proportion of IPD cases in <5yo by serotype: 2008

![Pie chart showing serotype distribution in <5yo IPD cases in 2008.](image)

TABLE 8. Recommended schedule for use of 13-valent pneumococcal conjugate vaccine (PCV13) among previously unvaccinated infants and children by age at time of first vaccination

<table>
<thead>
<tr>
<th>Age at first dose (mos)</th>
<th>Primary PCV13 series</th>
<th>PCV13 booster dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>2-6</td>
<td>3 doses</td>
<td>1 dose at 12-15 mos</td>
</tr>
<tr>
<td>7-11</td>
<td>2 doses</td>
<td>1 dose at 12-15 mos</td>
</tr>
<tr>
<td>12-23</td>
<td>2 doses</td>
<td>NA</td>
</tr>
<tr>
<td>24-59 in healthy children</td>
<td>1 dose</td>
<td>NA</td>
</tr>
<tr>
<td>24-71 in children with certain chronic diseases or immunocompromising conditions</td>
<td>2 doses</td>
<td>NA</td>
</tr>
</tbody>
</table>

Proportion of IPD cases caused by serotypes in different vaccine formulations, by age group: 2008

![Bar chart showing proportion of IPD cases caused by serotypes in different vaccine formulations.](image)
Revaccination with the 23-valent pneumococcal polysaccharide vaccine in middle-aged and elderly persons previously treated for pneumonia

Jan Töring*, Janne Heintz*, Helle Gjermoe Korsnes*, Åke Grysevich*

Abstract

Revaccination with the 23-valent pneumococcal polysaccharide vaccine (PPV) has received controversy due to lack of immunological data and fear of side effects. We re-vaccinated 42 elderly persons (median age 90 years) who had a history of hospital treatment for pneumonia, with PPV an average 19 years after their primary vaccination. Revaccination resulted in significant increase of the pneumococcal matrix antibody concentration (GMI) and the pneumococcal matrix antibody dilution (GMD), although to lower levels than after primary vaccination. Still, 76% of the persons responded with a GMD of $>1$ of an arbitrary titer. This re-vaccination was safe and induced a significant immune response in a majority of persons.

Hyporesponsiveness w/ PPSV23?

Comparison of Pneumococcal Conjugate Polysaccharide and Free Polysaccharide Vaccines in Elderly Adults: Conjugate Vaccine Elicits Improved Antibacterial Immune Responses and Immunological Memory

Advantages of conjugate over polysaccharide pneumococcal vaccines

- Immunologic priming & induction of immunologic memory
- Reduction in nasopharyngeal carriage
- Greater effectiveness against serotypes currently causing most invasive dz
- More effective against noninvasive syndromes including nonbacteremic pneumonia & otitis media
Back to our question
- The pharmacist calls & asks you to clarify which pneumococcal vaccine you want to give to this patient. How do you respond?
  A) 14-valent polysaccharide
  B) 23-valent polysaccharide
  C) 7-valent conjugate
  D) 13-valent conjugate
  E) I have no clue – just give what we normally give and don’t bother me…

Back to our patient
- 75 yo female smoker who lives at home with family. She has a history of DM 2, Afib & chronic systolic HF. She presents to the hospital c/o fever, sob & cough productive of rust-colored sputum. No history of hospitalization. Meds: metformin, lisinopril & coumadin.

T38.5 (101F) BP 143/77 HR 126 RR20 93%RA
Diaphoretic, crackles at L base; CXR=LLL infiltrate
Labs normal except for INR 1.7, BUN 25 mg/DL, BS 252 mg/DL

Next clinical question
- What should you recommend to the patient and her outpatient provider?
  A) Continue warfarin
  B) Stop warfarin and start aspirin
  C) Stop warfarin and start enoxaparin
  D) Stop warfarin and start fondaparinux
  E) Stop warfarin and start dabigatran
Atrial fibrillation

- Most common sustained arrhythmia – affects at least 2.3 million Americans
- By 2030, AF will affect est 4 million Americans
- AF is responsible for 15% of the 700K strokes in US each yr, resulting in $57.9 billion in annual direct & indirect costs

Risk of stroke in AF: CHADS2 Score

<table>
<thead>
<tr>
<th>Points</th>
<th>CHADS2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Congestive heart failure</td>
<td>1</td>
</tr>
<tr>
<td>Hypertension</td>
<td>1</td>
</tr>
<tr>
<td>Age 75 yrs or older</td>
<td>1</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>1</td>
</tr>
<tr>
<td>prior Stroke or TIA</td>
<td>2</td>
</tr>
</tbody>
</table>

CHADS2 score: annual stroke risk

<table>
<thead>
<tr>
<th>CHADS2</th>
<th>Stroke risk%</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>1.9</td>
<td>1.2-3.0</td>
</tr>
<tr>
<td>1</td>
<td>2.8</td>
<td>2.0-3.8</td>
</tr>
<tr>
<td>2</td>
<td>4.0</td>
<td>3.1-5.1</td>
</tr>
<tr>
<td>3</td>
<td>5.9</td>
<td>4.6-7.3</td>
</tr>
<tr>
<td>4</td>
<td>8.5</td>
<td>6.3-11.1</td>
</tr>
<tr>
<td>5</td>
<td>12.5</td>
<td>8.2-17.5</td>
</tr>
<tr>
<td>6</td>
<td>18.5</td>
<td>10.5-27.4</td>
</tr>
</tbody>
</table>
Anticoagulation in AF

• Warfarin has narrow therapeutic window
• ASA less effective than warfarin
• Clopidogrel & ASA more effective than ASA but less effective than warfarin
• SC idraparinux more effective than warfarin but incr bleeding risk
• Then we had ximelagatran…

Comparison of Ximelagatran with Warfarin for the Prevention of Venous Thromboembolism after Total Knee Replacement

Charles W. Francis, M.D., Scott D. Berlowitz, M.D., Philip C. Corr, M.D., Ph.D.,
Jae R. Leblanc, M.D., Jeffrey S. Ganzberg, M.D., Guy Parenteau, M.D.,
Gary R. Peters, M.D., Avier W. Roth, M.D., Jennifer McFarlin, M.S.,
and Clifford W. Culwell, jr., M.D., for the DISRUPT Study Group

CONCLUSIONS
The efficacy of oral ximelagatran, administered starting the morning after total knee replacement, was superior to that of warfarin for prevention of venous thromboembolism. Rates of hemorrhagic complications with the two drugs were similar.

Secondary Prevention of Venous Thromboembolism with the Oral Direct Thrombin Inhibitor Ximelagatran

Sam Schuitman, M.D., Katri Nikkila, M.D., Tarja Kankkunen, M.D.,
Solvag Billing Olsson, M.Sc., and Henry Eriksson, M.D.,
for the THRIVE II Investigators

CONCLUSIONS
Oral ximelagatran was superior to placebo for the extended prevention of venous thromboembolism. There was no significant increase in the frequency of bleeding complications, but there was an increase in the number of patients with a transient elevation in the alanine aminotransferase level.
# Dabigatran: RE-LY Trial

**Question:** Is dabigatran non-inferior to warfarin in the prevention of stroke & embolism due to afib?

**Design:** Multi-center randomized trial

Connolly SJ et al. NEJM 2009;361:1139-51

## RE-LY inclusion criteria

- Afib on EKG w/in past 6 mos plus at least one of following:
  - prev stroke or TIA
  - LVEF < 40%
  - NYHA class II or higher or HF sx w/in past 6 mos
  - > or = 75yo or 65 to 74 yo w/ DM, htn or CAD

## RE-LY exclusion criteria

- Severe heart-valve disorder
- Stroke w/in 14 day days or severe stroke w/in past 6 mos
- Condition which incr risk of hemorrhage
- CRcL , 30ml/min
- Active liver disease
- Pregnancy
RE-LY Trial Results

% Time INR in therapeutic range

- RE-LY: 64%
- ACTIVE: 64%
- SPORTIF: 66-68%

Cost-Effectiveness of Dabigatran Compared With Warfarin for Stroke Prevention in Atrial Fibrillation

- Study estimates: dabigatran $364/mo
- Total costs (over 35 yrs)
  - Warfarin: $143,193
  - Dabigatran 110mg: $164,576
  - Dabigatran 150mg: $168,398
"In pts 65 yrs & older w/ nonvalvular AF at incr risk for stroke, dabigatran may be a cost-effective alternative to warfarin depending on pricing in the United States."

Dabigatran: FDA Indication
- Reduce risk of stroke & systemic embolism in pts w/ non-valvular afib
- Dosing:
  150mg orally BID w/ or w/out food
  Capsules should be swallowed whole. Any breaking of the capsules can increase exposure.
  Avoid all lapses in therapy

Dabigatran: Dosing adjustments
<table>
<thead>
<tr>
<th>Est CrCL (ml/min)</th>
<th>Dosing</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;30</td>
<td>No dose adjustment</td>
</tr>
<tr>
<td>15-30</td>
<td>75mg BID</td>
</tr>
<tr>
<td>ESRD (&lt;15), HD</td>
<td>No recommendation</td>
</tr>
</tbody>
</table>
Convert from Warfarin to Dabigatran

- Stop Warfarin and start Dabigatran when INR is below 2

Convert from Dabigatran to warfarin

<table>
<thead>
<tr>
<th>Est CrCL (ml/min)</th>
<th>When to start warfarin</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt; 50</td>
<td>3 days before DC Dab</td>
</tr>
<tr>
<td>31 to 50</td>
<td>2 days before DC Dab</td>
</tr>
<tr>
<td>15 to 30</td>
<td>1 day before DC Dab</td>
</tr>
<tr>
<td>&lt;15</td>
<td>No recommendation</td>
</tr>
</tbody>
</table>

Dabigatran: Convert to parenteral anticoagulants

- For pts currently taking Dabigatran, wait 12 hrs (CrCl >/= 30) or 24 hrs (CrCl < 30) after the last dose of Dabigatran before starting treatment with a parenteral anticoagulant.
**Dabigatran: Convert from parenteral anticoagulants**

- For pts receiving a parenteral anticoagulant, start Dabigatran 0-2 hrs before the time the next dose of drug was due.
- Start Dabigatran at the time of discontinuation of intravenous UF heparin

**Dabigatran: Drug interactions**

- Avoid concomitant use with P-gp inducers (e.g. rifampin): reduces dabigatran levels
- No dose adjustments necessary with these P-gp inhibitors (e.g. ketoconazole, verapamil, amiodarone, quinidine & clarithromycin). Do not extrapolate this recommendation to other P-gp inhibitors

**Dabigatran: Overdosage**

- There is no antidote

  In event of bleeding complications...

- Maintain diuresis (it is excreted in urine)
- Hemodialysis removes 60% drug in 2-3 hrs
- Consider surgical hemostasis or transfusion w/ FFP or PRBCs
- Measurement of aPTT or ECT may guide therapy
Back to our patient

- 75 yo female smoker who lives at home with family. She has a history of DM 2, Afib & chronic systolic HF. She presents to the hospital c/o fever, sob & cough productive of rust-colored sputum. No history of hospitalization. Meds: metformin, lisinopril & coumadin

T38.5 (101F)  BP 143/77  HR 126  RR 20  93% RA
Diaphoretic, crackles at L base;
CXR=LLL infiltrate
Labs normal except for INR 1.7, BUN 25 mg/DL, BS 252 mg/DL

Back to our clinical question

- What should you recommend to the patient and her outpatient provider?
  A) Continue warfarin
  B) Stop warfarin and start aspirin
  C) Stop warfarin and start enoxaparin
  D) Stop warfarin and start fondaparinux
  E) Stop warfarin and start dabigatran
References

- **Tocilizumab**

- **Pegloticase**

- **Tesamorelin**

- **Fingolimod**

- **Pneumococcal (PCV-13) conjugate vaccine**

- **Ceftaroline**
References

- Dabigatran