# Switching patients to new regimens; The role of the pharmacist

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# Disclosures

None

# Patient MA

61year old female

Born in Malawi - lived in UK for past 40 years

**PMH**

- HIV–1 diagnosed 1999
- Hypertension
- AF
- Osteoporosis
- Hep A & Hep B immune

| Bloods | |
|---|---|
| Nadir CD4 (1999) | 157 (9%) |
| Most recent CD4 (2019) | 605 (29%) |
| Viral load at start (1999) | 56,000 |
| Baseline VRT | Wildtype |
| Most recent VL (2019) | 28 |

**Current ARV regimen**:

Darunavir/ritonavir monotherapy

- Previously on Truvada NVP - stopped due to raised LFTs

**DHx**

- Ramipril
- Warfarin

# Background

- Pt attends pharmacy requesting an emergency supply of medication
- On questioning discover that she is running out of meds as she missed her appointment due to a hospital admission
- Admitted to local hospital with chest pain three weeks ago and diagnosed with NSTEMI - 4 day admission

During Admission

- Warfarin stopped and switched to rivaroxaban
- Started on clopidogrel
- Didn’t tell medics/nursing staff she was HIV+ve as she knew some of the staff in the hospital

# Drug-Drug Interactions!!!!!

| Do Not Coadminister |
| --- |
| Darunavir + ritonavir |
| Clopidogrel |

| Do Not Coadminister |
| --- |
| Darunavir + ritonavir |
| Rivaroxaban |

- Contraindicated interaction
- Could switch DOAC/Antiplatelet
  - ? Aspirin
  - ?Edoxaban – weight an issue
- Could switch ARVs
  - Pt stable – nil side effects, undetectable VL

# Dual Therapy?

Is this an option?

Remember the patient

- High CV risk - ? Abacavir
- Confirmed Osteoporosis - ? TDF
- Baseline VRT=WT
- INSTI naive
- Potential for further co –morbidities and polypharmacy

# Durable Suppression 2 Years After Switch to DTG + RPV 2-Drug Regimen: SWORD-1 and SWORD-2 Studies THPEB047

Aboud M,[1] Orkin C,[2] Podzamczer D,[3] Bogner J,[4] Baker D,[5] Khuong-Josses M-A,[6] Parks D,[7] Angelis K,[8] Kahl L,[1] Blair E,[9] Underwood M,[9] Wynne B,[10] Vandermeulen K,[11] Gartland M,[9] Smith K[9]

[1]ViiV Healthcare, Brentford, UK; [2]Barts Health NHS Trust, London, UK; [3]Hospital Universitari de Bellvitge, Barcelona, Spain; [4]Hospital of the University of Munich, Munich, Germany; [5]East Sydney Doctors, Darlinghurst, Sydney, Australia; [6]CHG - Hôpital Delafontaine, Saint Denis Cedex, France; [7]Central West Clinical Research, St Louis, MO, USA; [8]GlaxoSmithKline, Uxbridge, UK; [9]ViiV Healthcare, Research Triangle Park, NC, USA; [10]ViiV Healthcare, Collegeville, PA, USA; [11]Janssen Pharmaceutica NV, Beerse, Belgium

**48-WEEK RESULTS**

TANGO

**96-WEEK RESULTS**

gemini 1 gemini

Suitable to treat HIV-1 infection only in adults with no known or suspected resistance to integrase inhibitors or lamivudine.

# Outcome

- Switched to DTG/3TC
  - Counselled on potential DDIs with mineral containing supplements
- Returned for follow up two months later
  - VL remained undetectable
  - Some ADRs after initiating – sleep disturbance, now resolved
- Important Learning Point
  - Patient counselling on DDIs is an essential part of every HCP consultation
  - Don’t just focus on current medication with little thought on potential future medication and DDIs

# Case 2

# TF, 31 year old man

Background

- ~~Advanced HIV, CD4 10~~
- 4 months fever, night sweats, weight loss & transient rashes
  - KS and low level CMV viraemia
  - Multiple Ix – cause PUO not identified
  - Rx for PCP (empiric)
- Started ART (TRU, DRV/r, RAL) 9/7
  - VL: > 2 million (no resistance) → 8000 copies/ml (2 weeks)
  - Fevers worse, abdo pain
  - Anaemia, thrombocytopenia, ↑ALP, ↑ferritin, normal renal function
  - U/S: hepatosplenomegaly
  - Finally……MAI grown on B/C from last admission (and sputum)
- Admitted to start MAI Rx / Change ART - plan
  - Sensitive to clari
  - Amik 7/5mg/kg, Rifabutin, Clari & Ethambutol
  - Truvada & dolutegravir

# Admission 19/7

Noted to have AKI (stage 3) - new:

- Urgent renal U/S: normal
- Fluid resuscitation / frusemide

Over next 24-48 hours:

- Fluid resuscitation / frusemide
- Cefuroxime
- Progressive renal failure
- Compensated metabolic acidosis

Admitted to ICU 21/7 for haemo-filtration

# ART prescription

On haemofiltration
CrCl: 39ml/min

| | 20/7 | 21 | 21 | 22 | 23 | 24 |
|---|---|---|---|---|---|---|
| | T8 | T8 | ICU | ICU | ICU | ICU |
| **Truvada** | W | S | | | | |
| **Dolutegravir 50mg od** | | | NP | NP | NP | NP |
| **Raltegravir 400mg bd** | ** | * Am S | NP | NP | NP | NP |
| **Drv/rit 800mg/100 mg od** | * | | * | * | * | * |
| **3TC 150mg** | * | | NP | | | |
| **3TC 100mg** | | | | | | |
| **3TC 50mg** | | | NP | P | * | * |

- 20/7: DRV/r, 3TC (renal dose), DTG (ie stop TDF & switch RAL)
- 21/7: ID consultant W/R (on ward) – switched to DRV/r monotherapy in view of ARF
- 22/7: Consultant W/R note
  - reintroduce 3TC – 50mg given – under-dosing given CrCl on haemofiltration
- Effectively on dual therapy (bPI & 3TC)
  - Very high VL on commencing ART (>1 million) & still viraemic on admission (8-11,000 copies/ml)
  - Three drugs preferable
    - DTG
    - ? Kivexa (HLAB5701 neg

On haemofiltration
CrCl: 39ml/min

| | 21 | 22 | 23 | 24 | 25 | 26 | 27 | 28 | 29 | 30 | 31 | 1/8 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | ICU | ICU | ICU | ICU | ICU | ICU | ICU | ICU | ICU | ICU | ICU | ICU |
| | | | | | | | | | | | | |
| **Amikacin** | | * | * | * | * | * | * | * | * | * | * | * |
| **Clarithro 500mg bd** | * pm | * | * | * | * | * | * | * | * | * | * | * |
| **Ethambutol 1200mg, daily** | * | * | * | * | * | * | * | * | * | * | * S | |
| **Ethambutol 1200mg, M, W, F** | | | | | | | | | | | P | * |
| **Rifabutin 450mg** | *1 | * | * | * | * | * | * | * | * | * | * | |
| **Rifabutin 300mg** | | | | | | | | | | | P | * |

# MAI prescription

- ID consultant W/R 21/7 (on ward):
  - give rifabutin, clari, ethambutol once on haemofiltration (hold amik)
- ID consultant W/R 22/7 (ICU):
  - start amikacin
- Rifabutin dose:
  - Correct for haemofiltration
  - Doesn't account for DI with bPI & clarithromycin
  - 150mg appropriate at this stage
  - Potential side effects from 'overdose' rifabutin: neutropenia, ↓platelets, hepatitis, uveitis, arthralgia
- Would azithromycin have been preferable to clarithromycin?

On HF

**CrCl**: 27ml/min

**CrCl**: 13 ml/min

**CrCl:** >30ml/min

| | 28 | 29 | 30 | 31 | 1/8 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | TTA |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | ICU | ICU | ICU | ICU | ICU | ICU | ICU | ICU | ICU | ICU | T8 | T8 | T8 |
| Truvada | | | | | | | | | | | | | |
| Dolutegravir 50mg od | NP | NP | NP | P | * | * | * | * | * | * | * | * | * |
| Raltegravir 400mg bd | | | | | | | | | | | | | |
| Drv/rit 800mg/100mg od | * | * | * | S | | | | | | | | | |
| 3TC | | | | | | | | | | | | | |
| 3TC 150mg | | | | | | | | | | | | | * |
| 3TC 100mg | | | | | | | | | | | R | | |
| 3TC 50mg | * | * | * | * | * | * | * | * | * | W | | | |
| Abacavir 600mg | | | | | | | | | | | | | * |
| | | | | | | | | | | | | | |
| Amikacin | * | * | * | * | * | * | * | * | * | * | * | * | |
| Clarithro 500mg bd | * | * | * | * | * | * | * | * | * | * am<br>W pm | * | * | * |
| Ethambutol 1200mg, daily | * | * | * | *<br>S | | | | | | | | | * |
| Ethambutol 1200mg, M, W, F | | | | P | * | | * | | | * | | * | |
| Rifabutin 450mg | * | * | * | * | | | | | | | | | |
| Rifabutin 300mg | | | | P | * | * | * | * | * | * | * | * | * |

# Prescribing decisions post HF

**MAI Rx:**

- Ethambutol dose reduced to 3x/week on 31/7 – 8/8 (daily on TTA)
  - necessary?
- Rifabutin reduced to 300mg on 1/8 (when DRV/r stopped)
  - wash out period 4-5 days….

**ART:**

- MDT 30/7:
  - DI between DRV/r, rifabutin, clari noted
  - Not on DTG
  - DRV/r switched to DTG on 31/7
- 3TC – correct dose on discharge
- Abacavir added on discharge

# Potential harms?

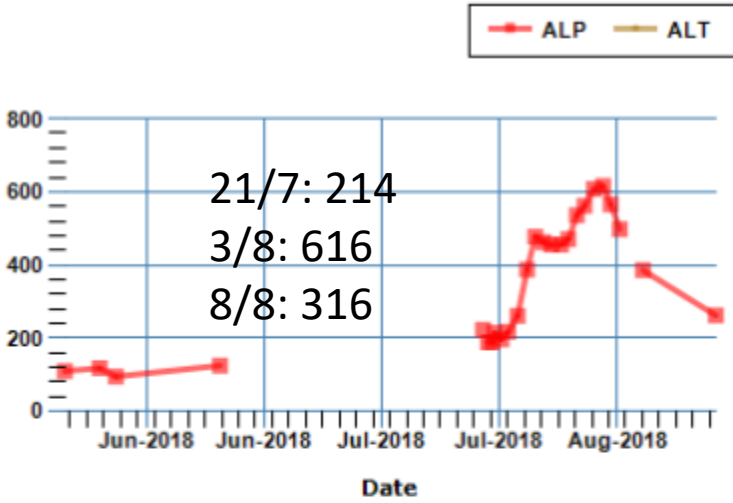
Patient developed

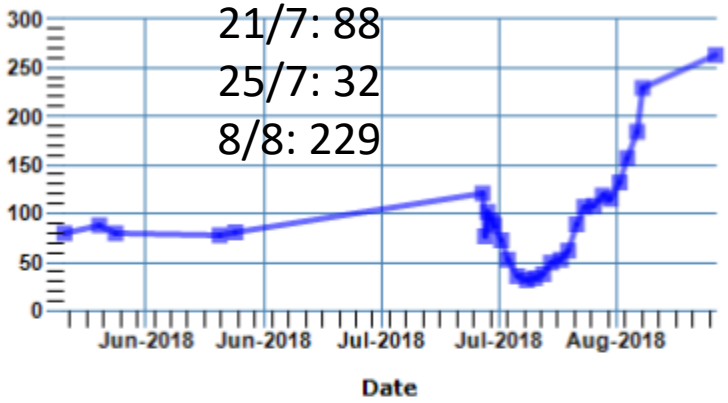
1. Resistance to 3TC & DTG
   - 3TC dose remained at 150mg OD post d/c for 5 weeks
   - 3 months post d/c (pt now on triumeq) VL increased to 218,776
     - New M184V and R263K
2. Hepatitis on ICU
3. Anaemia and thrombocytopenia on ICU

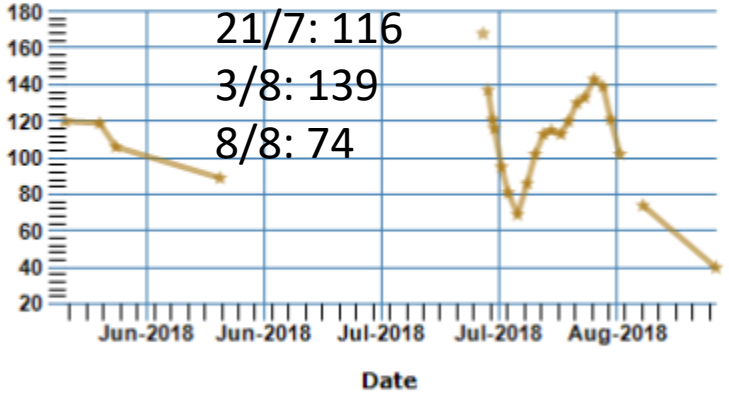
Pt switched to Truvada DRV/r DTG BD – Nov 18

- Last VL undetectable in July 2019
- Just completed MAI treatment

Unclear adherence post discharge



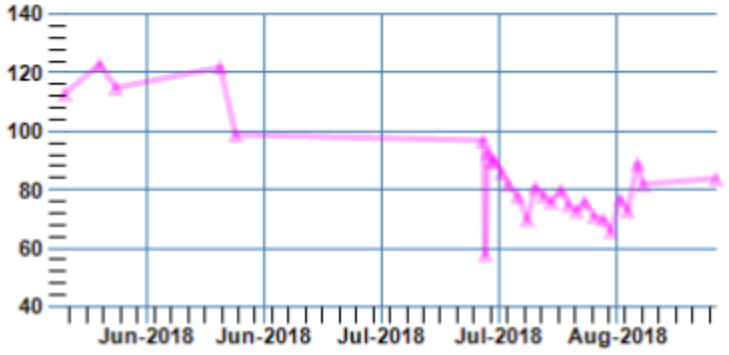




Hepatitis:
- MAI
- MAI / IRIS?
- Did rifabutin play a part?

Multi-factorial

Thrombocytopenia

Multi-factorial



# Learning Points

Unclear if rifabutin ‘overdosing’ was a significant contributing factor in hepatitis / thrombocytopenia – both were multifactorial

Unclear to what extent prescribing decisions contributed to development of resistance; other factors may also have played a role

- Evidence used to make dosing decisions in patients with renal failure are based on patients with CKD not AKI
- 3TC under-dosing: debate amongst expert to the extent to which CrCl calculations in patient with AKI on haemofiltration are correct
- Don’t forget about the role of DTG and serum Cr increase
- Complex severely immunocompromised patients should have as robust a regimen as possible – with retrospect there was scope to improve this patients ART choices

# Thank you for listening!

Any Questions?