


A Case of HIV with Multiple Related Infections- Balancing Treatments, Drug Interactions and Side-effects

Talia James

*Basic Physician Trainee
Royal Perth Hospital, WA*



Mr K

- HIV
 - 55M diagnosed in 2005
 - HLA B5703 positive
 - Long term slow progressor. Not on ART

- PMH: Essential Hypertension, Malaria, Typhoid fever

- SHx
 - Arrived in 2005 from Cote d'Ivoire
 - Works as a baker and pastry chef
 - Has a wife and 3 children

- Last seen in the Immunology clinic in 2011 with CD4 442, VL 12800 cp/ml

Admission October 2017

- ▀ Presented with collapse, fevers and weight loss
- ▀ Examination
 - ▀ Unwell, thin
 - ▀ Temp 38.8 C
 - ▀ Chest clear, Abdomen soft, no organomegaly
 - ▀ Painful 2cm left supraclavicular lymph node

Investigations

| | | | | |
|-------|------|--|-------------|------|
| Hb | 73 | | bili | 10 |
| WCC | 5.38 | | ALT | 40 |
| Plt | 226 | | ALP | 112 |
| MCV | 76 | | GGT | 151 |
| Neut | 4.8 | | alb | 23 |
| Lymph | 0.11 | | | |
| CRP | 280 | | LDH | 1130 |
| INR | 1.2 | | Hapto | 6.99 |
| U&E | NAD | | ferritin | 1930 |
| | | | iron | 2 |
| | | | transferrin | 14 |
| | | | T.sat | 7 |

Investigations

- ▶ Lymph node biopsy: positive for **Acid fast bacilli**
- ▶ Blood and urine cultures positive for **Mycobacteria TB**
- ▶ Toxoplasma serology: positive IgG
- ▶ **CT Abdo/Pelvis:** bilateral supraclavicular lymphadenopathy, enlarged LN around porta hepatis, SMA and para-aortic
- ▶ **CT brain and MRI brain:** no evidence of intracranial mass or infection

Disseminated TB

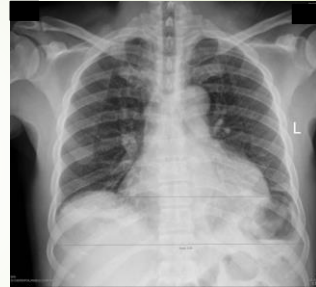
Other issues....

- ▶ **Advanced HIV**
 - ▶ CD4 absolute count 5 (1%), VL 79433
- ▶ **Hepatitis B coinfection**
 - ▶ Viral load: 2×10^7 IU/ml, HBcAb & sAg positive, HBeAg neg
 - ▶ Treatment naive
 - ▶ US abdomen 18 Oct: normal

Other issues....

- ▶ **Moderate to large pericardial effusion**

- ▶ Secondary to TB. No drainage required
- ▶ For repeat ECHO in 2 and 6 weeks prior to initiation of ART to monitor size given risk of IRIS



- ▶ **TB retinitis and HIV retinopathy**

- ▶ Nil visual symptoms reported
- ▶ O/E: subretinal nodules, patchy, poorly defined opacities consistent with TB retinitis.
- ▶ For ongoing review

Other issues....

- ▶ **Opportunistic infections/prophylaxis**

- ▶ Fluconazole 50mg PO for oral candidiasis
- ▶ G6PD screening test indicated possible deficiency therefore co-trimoxazole and dapsone avoided - Pentamidine nebulisers for PJP prophylaxis

The challenge

- Disseminated TB
- Advanced HIV
- Hepatitis B
- Pericardial effusion secondary to TB
- TB retinitis/HIV retinopathy
- Oral candidiasis
 - Fluconazole
- PJP prophylaxis
 - Pentamidine

The challenge

- Disseminated TB
- Advanced HIV
- Hepatitis B
- **Pericardial effusion secondary to TB**
- **TB retinitis/HIV retinopathy** ← Steroids to prevent TB-IRIS
- Oral candidiasis
 - Fluconazole
- PJP prophylaxis
 - Pentamidine

The challenge

- Disseminated TB
- **Advanced HIV** ← Needs to be treated prior to initiation of steroids
- **Hepatitis B**
- Pericardial effusion secondary to TB ← Steroids to prevent TB-IRIS
- TB retinitis/HIV retinopathy
- Oral candidiasis
 - Fluconazole
- PJP prophylaxis
 - Pentamidine

The challenge

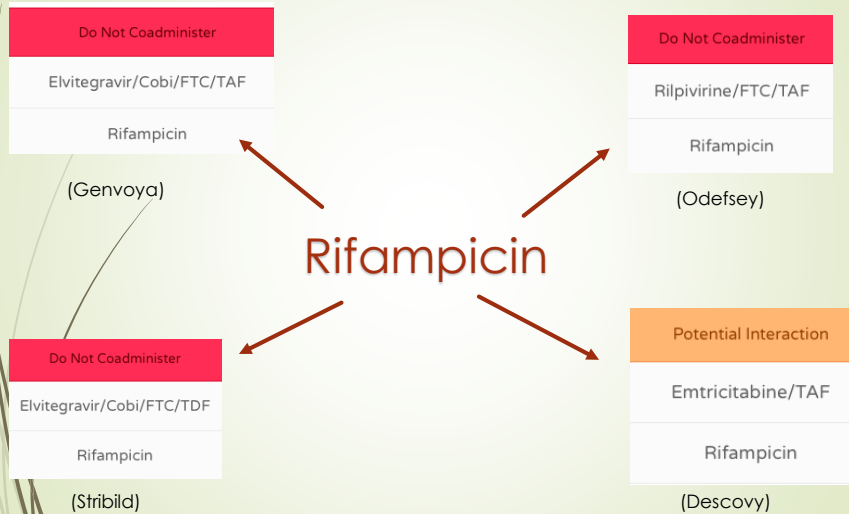
- **Disseminated TB** ← Treat prior to initiation of antivirals
- Advanced HIV ← Treat prior to initiation of steroids
- Hepatitis B
- Pericardial effusion secondary to TB ← Steroids to prevent TB-IRIS
- TB retinitis/HIV retinopathy
- Oral candidiasis
 - Fluconazole
- PJP prophylaxis
 - Pentamidine

Treatment

- **Mycobacterium tuberculosis**
 - Commenced Rifampicin, Isoniazid, Pyrazinamide, Ethambutol and pyridoxine (day 0)
- **HIV and Hepatitis B**

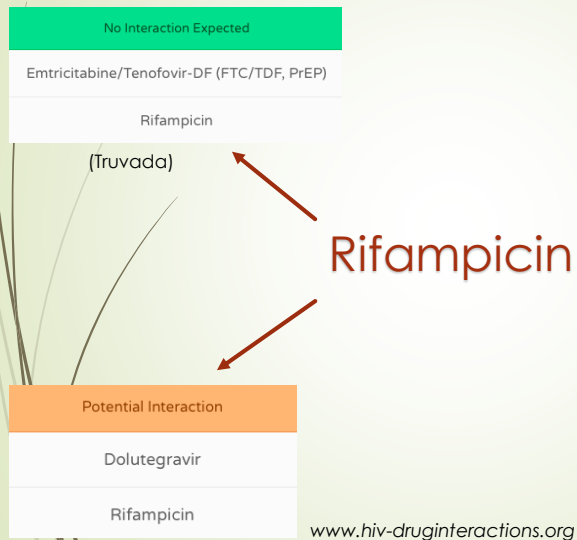
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Drug Interactions



www.hiv-druginteractions.org

Drug Interactions



Clinic Review (day 19)

- **Mycobacterium tuberculosis**
 - (day 0) Commenced Rifampicin, Isoniazid, Pyrazinamide, Ethambutol and pyridoxine
- **HIV and Hepatitis B**
 - (day 19) Tenofovir disoproxil fumarate/emtricitabine (Truvada)
 - Dolutegravir 50mg **BD**
- **Preventing TB-associated IRIS affecting pericardium and eye**
 - Planned for Prednisolone 75mg (day 21)

Drug Interactions

| No Interaction Expected |
|--|
| Emtricitabine/Tenofovir-DF (FTC/TDF, PrEP) |
| Rifampicin |

Prednisolone

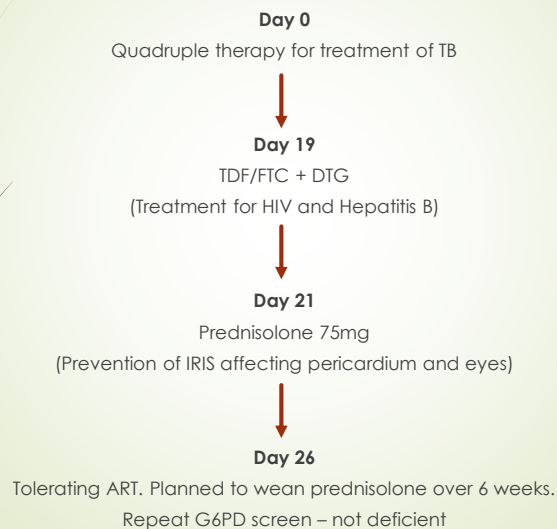
- rifampicin increases the plasma clearance of prednisolone by ~50%

Rifampicin

| Potential Interaction |
|-----------------------|
| Dolutegravir |
| Rifampicin |

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Summary

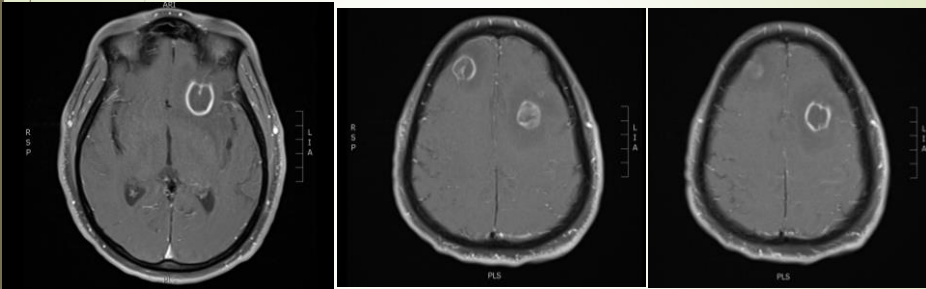


Admission November 2017

- Day 31 after commencing TB treatment
- Day 12 after commencing ART

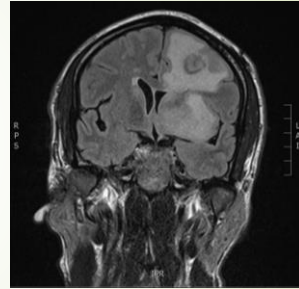
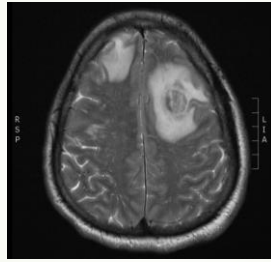
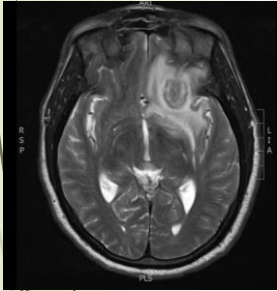
- Presented with fever
- O/E:
 - Looked well
 - Supraclavicular and cervical lymphadenopathy
 - Chest clear, Abdominal examination unremarkable
 - Cranial and peripheral nerve examination NAD
- **Unable to recall simple details. Apraxia**

Axial (T1 post contrast)



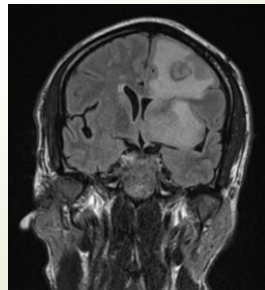
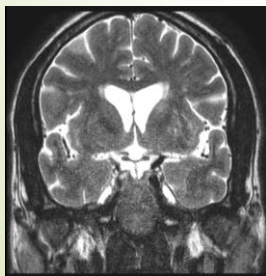
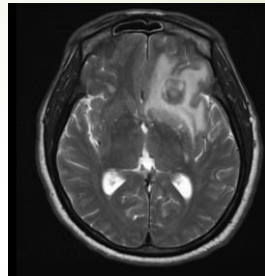
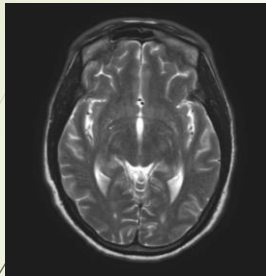


T2 flair



October

November



Cerebral toxoplasmosis (unmasking IRIS)

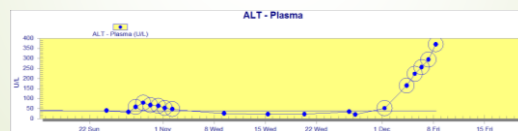
- ▀ Sulfadiazine 1g QID
- ▀ Pyrimethamine (200mg stat then 75mg OD)
- ▀ Ca folinate 15mg OD

- ▀ Dexamethasone 8mg QID

Week 6

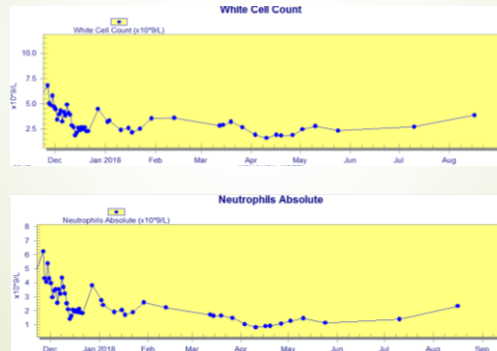
- ▀ Clinically improving but....

| UNIT / ANALYSIS | 15.11 | 22.11 | 29.11 | 06.12 | 13.12 | 20.12 | 27.12 | 03.01 | 10.01 | 17.01 |
|--------------------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|
| ALT - Plasma (U/L) | | 4 | | 4 | 10 | 10 | 10 | 10 | 10 | 10 |
| AST - Plasma (U/L) | | 1 | | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| ALP - Plasma (U/L) | | 1 | | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| Gamma-GT (U/L) | | 1 | | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| Urea (mmol/L) | | 4 | | 4 | 4 | 4 | 4 | 4 | 4 | 4 |
| Cr (mmol/L) | | 0.1 | | 0.1 | 0.1 | 0.1 | 0.1 | 0.1 | 0.1 | 0.1 |



Week 6

- Clinically improving but....



Side-effects

Hepatotoxicity

- **Hepatitis B IRIS flare?**
 - Hepatitis D serology negative
 - Viral load 2×10^6 IU/mL (Initial viral load 2×10^7 IU/L)
- **Drug-induced?**
 - Isoniazid
 - Pyrazinamide
 - Rifampicin
 - Sulfadiazine
 - Pyrimethamine
 - Fluconazole

Bone marrow suppression

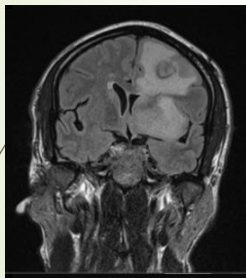
- Pyrimethamine
- Sulfadiazine
- Truvada
- Rifampicin

Week 6

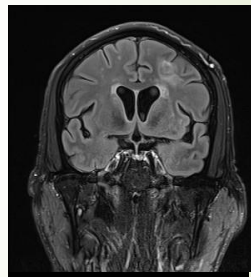
- TB treatment
 - Rifampicin, Isoniazid, Pyrazinamide
 - 1 week later started amikacin, ethambutol and moxifloxacin
- Cerebral toxoplasmosis treatment
 - ~~Sulfadiazine~~ Commenced clindamycin 600mg QID.
 - Pyrimethamine dose reduced to 50mg

Week 10 of TB Treatment
Week 6 of treatment for toxoplasmosis

Before

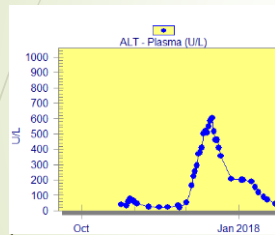


6 weeks of treatment
for cerebral toxoplasmosis



MRI brain T2 flair

Week 10 of TB Treatment
Week 6 of treatment for toxoplasmosis



HIV viral load <40 cp/ml
CD4 count 12

Hepatitis B viral load 8.8×10^5 IU/ml

Week 10-12

- TB treatment
 - Amikacin ethambutol and moxifloxacin
 - Re-introduction of rifampicin followed by isoniazid
- Cerebral toxoplasmosis treatment
 - Clindamycin 600mg QID.
 - Commenced on secondary prevention with sulfadiazine 1g bd and reduced dose pyrimethamine 25mg OD

Week 16

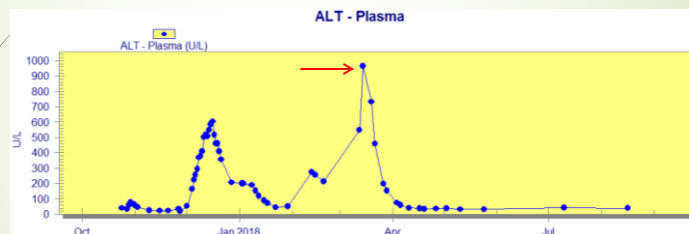
Medications

- ▶ Rifampicin
- ▶ Isoniazid
- ▶ Sulfadiazine
- ▶ Pyrimethamine
- ▶ Calcium folinate
- ▶ Pyridoxine
- ▶ TDF/FTC
- ▶ Dolutegravir
- ▶ Amlodipine

Ceased medications

- ▶ Dexamethasone
- ▶ Prednisolone
- ▶ Moxifloxacin
- ▶ Ethambutol
- ▶ Clindamycin

Hepatotoxicity (Month 5)



Hepatotoxicity (Month 5)

- TB treatment
 - Rifampicin and isoniazid ceased
 - ALT settled from 965 to 199.
 - Rifampicin and moxifloxacin 400mg OD restarted 2 weeks later
 - ALT continued to fall to 41
 - Isoniazid suspected of causing hepatotoxicity.

- Cerebral toxoplasmosis secondary prevention
 - ~~Sulfadiazine and pyrimethamine~~ switched to Bactrim DS 1 tab bd

Progress

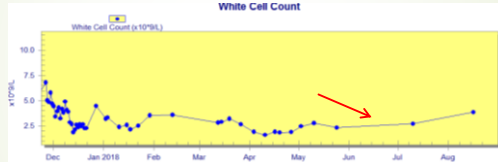
- Month 6
 - Continued leucopenia on Bactrim DS. Changed to atovaquone 750mg tds

- Month 7
 - Ethambutol re-commenced. Continued rifampicin and moxifloxacin

- Month 9
 - Completed TB treatment with rifampicin, moxifloxacin and ethambutol

Progress

- Since rifampicin ceased, WCC improved



- ~~Atevaquone~~ ceased. Bactrim DS re-started

How is Mr K?

- Completed 9 months of TB treatment
- Completed primary treatment for cerebral toxoplasmosis
- Continues treatment for HIV, Hepatitis B (TDF/FTC + DTG)
- Continues secondary prophylaxis (Bactrim)
- CD4 count 128
- HIV viral load <40 cp/ml
- Hepatitis B viral load NOT detected

How is Mr K?

- Back to full time work
- His wife delivered a healthy baby boy!

Plan 27th September 2018

Medications

- Genvoya
- Co-trimoxazole
- Amlodipine

Ceased medications

- Dexamethasone
- Clindamycin
- Prednisolone
- Pyrimethamine
- Sulfadiazine
- Calcium folinate
- Isoniazid
- Pyridoxine
- TDF/FTC
- Dolutegravir
- Rifampicin
- Moxifloxacin
- Ethambutol
- Atovaquone
- Fluconazole



Conclusion

- Case highlights that despite huge advances in treatment, complex cases do still present with the same issues of co-infections, drug interactions and side effects
- Important reminder of starting treatment at the point of diagnosis



Acknowledgements

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Mr K

