UPDATES ON HIV IN THE HOSPITAL

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No disclosures or conflicts
• OI incidence has declined but is this the whole story?
  • Outpatient HOPS cohort (USA) →
  • Data from national hospital discharge survey (NHDS) suggest a somewhat different view
OI DECLINE: THE WHOLE STORY?

- OI decline less dramatic
- 2 main HIV-infected groups:
  - Aware of HIV and receiving ART
  - Unaware of HIV / aware not in care
- In 2014, an estimated 44,000 in the US were newly infected

Kamimoto Natl HIV Prevention Conference 2011

Slide adopted with permission from H Masur
GLOBALLY: OI AND OTHER HOSPITALIZATIONS IN ADULTS WITH HIV

- Globally late care presentation remains important cause of hospitalization + death
- Currently only ½ of HIV patients are receiving ART at the time of admission
- Cancers and NCDs rising in PLHIV but OIs and bacterial infections still the main cause of mortality in hospitalized HIV patients in Africa
- In-hospital mortality 31%

Causes of mortality in HIV patients admitted to hospital, globally

Ford et al Lancet HIV 2015
OI Updates
Pneumocystis pneumonia update
PCP IN AFRICA

• PCP once thought less common but more likely issue inadequate diagnostic capacity

• Recent systematic review of PCP in Africa revealed:
  • Median CD4 of patients with PCP 48 cells/ul
  • PCP prevalence: 24% of inpatients presenting with respiratory illness and 5% of outpatients
  • Beware! Coinfections common in PCP patients
  • Empirical PCP treatment justified in advanced HIV + PCP syndrome & poor response to initial Rx

• Overall mortality 18%

• Prevalence may be declining but still important OI in those presenting late

Co-existent opportunistic disease (%; 95% CI)
- Overall 29.3 [25.4–33.6] (26 studies, n = 474)
- Tuberculosis 14.8 [11.8–18.5] (25 studies, n = 431)
- Bacterial pneumonia 8.7 [0.6–11.8] (22 studies, n = 445)
- Pulmonary cryptococcosis 1.4 [0.4–3.6] (17 studies, n = 283)
- Pulmonary Kaposi sarcoma 4.1 [2.4–6.6] (21 studies, n = 410)

Wasserman et al. BMC Infectious Diseases (2016)
CORTICOSTEROIDS IN PCP: AN RCT OF PREDNISONE V. PLACEBO IN PCP

TMP-SMX remains treatment of choice

What about the role of steroids?

- Primary outcomes: respiratory failure or death
- About 80% received TMP-SMX at 15-20 mg/kg/day
- Results at 31d f/u:
  - Respiratory failure 14% vs. 30%, death 16% vs. 26% (p=0.026), both favoring prednisone

Recommendation:

Steroids if PaO2 <70 mm Hg or A-a gradient >35

That is a saturation of 93% or less

Regimen: 21 days

- Prednisone 40mg q12 (day1-5), 40mg/day (day 6-10), 20 mg/day (days 11-21) ** or **
- Methylprednisone IV at 75% of predn. dose

Sattler et al NEJM, 1990
PCP IN ICU

- Respiratory decompensation common 48-72 hours into PCP treatment
- About 10% require mechanical ventilation (MV) and another 10% noninvasive positive pressure ventilation
- Early in US epidemic there was reluctance to use MV
  - Survival in HIV patients with resp. failure from PCP requiring MV was ~20%
- DHHS guidelines endorse MV “if functional status is such that it would be otherwise appropriate,” as with HIV uninfected.

WHAT IS THE MODERN SURVIVAL IN HIV-ASSOCIATED PCP WITH RESP. FAILURE REQUIRING MECHANICAL VENTILATION?

• 0%
• 5%
• 20%
• 40%
Overall the survival for PCP patients requiring mechanical ventilation has improved to ~40-50%.

- Use of corticosteroids in severe PCP widespread since 1990s so unlikely the cause
- New approaches to ventilating patients may have played a role
- A higher proportion of patients admitted with PCP are receiving or initiating ART in hospital

<table>
<thead>
<tr>
<th>Year</th>
<th>Setting</th>
<th>Survival</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre 2000</td>
<td>Multiple</td>
<td>~20%</td>
</tr>
<tr>
<td>2000</td>
<td>USA</td>
<td>44%</td>
</tr>
<tr>
<td>2006</td>
<td>UK</td>
<td>62%</td>
</tr>
<tr>
<td>2007</td>
<td>Thailand</td>
<td>57%</td>
</tr>
<tr>
<td>2008</td>
<td>France</td>
<td>85%</td>
</tr>
<tr>
<td>2014</td>
<td>China</td>
<td>60%</td>
</tr>
</tbody>
</table>

* Brazil retrospective study: Survival in PCP patient admitted to ICU better among among those initiating ART during ICU stay vs. those not receiving ART in hospital.

Miller et al Thorax 2006
Morris A et al AIDS 2003
Croda et al Crit Care Med 2009
FALLING MORTALITY OF PCP IN ICU

• A 2000 study showed improved mortality in all patients with ARDS using ventilation with low tidal volumes (TV)
  • San Francisco (2009): Survival of HIV patients with acute lung injury (PCP 36% of cohort) on MV better with low TVs.

• Italian study: Non-invasive positive pressure ventilation can avoid intubation in some PCP patients; those avoiding intubation have improved outcome
  • Included: PCP with acute respiratory failure
  • Excluded: shock, respiratory arrest, altered MS
  • 3/38 did not tolerate NIPPV and required MV but intubation avoided in 66% of NIPPV for whom survival was superior (100% vs. 38%; P=0.003) and few PTX.

Davis et al Thorax 2009

ARDSNet Study 2000 NEJM

Confalonieri Intensive Care Med 2002
Cryptococcal meningitis updates
HOW COMMONLY IS THE CSF CULTURE POSITIVE AFTER 2 WEEKS OF AMPHOTERICIN-BASED THERAPY?

1. 5%
2. 20%
3. 50%
4. 90%
CRYPTOCOCCAL MENINGITIS

- Viable *Cryptococcus neoformans* present in 50% at end of amphotericin treatment
- Positive culture at end of induction associated with poor outcomes including incr. risk of IRIS and mortality
  - In SA, hi mortality linked with (+) CSF culture end of consolidation (14% mortality sterile CSF vs 26%)
- In the COAT trial, fluconazole 800 mg/day – not 400 mg/day – was given as consolidation therapy
- High dose fluconazole consolidation appeared to improve outcomes in culture (+) patients
- Without routine cultures, optimal duration of high dose fluconazole remains unclear

Rolfes et al Open Forum ID 2015
ACCESS TO FLUCYTOSINE FOR CM

- Induction therapy in South Africa: amphotericin B + fluconazole
- In large trial, mortality higher among patients receiving amphotericin B + fluconazole vs. amphotericin B + flucytosine
- Flucytosine is an old, generic antifungal drug (1957).
  - It is not highly toxic or difficult to monitor at doses used in CM

Barriers:
- (1) Not registered in most of Africa; previously marketed in SA by Roche
- (2) Current FDA-approved sources are very expensive with 2 generic producers
- (3) Market failure of insufficient supply of an old generic drug

Day JN et al NEJM 2013
Govender et al SAMJ 2014
ADJUNCTIVE DEXAMETHASONE IN CM?

Mortality in some types of meningitis is improved with corticosteroids

- This trial in SE Asia and Africa randomized HIV-infected patients treated with CM receiving amphotericin + fluconazole to tapering dexamethasone or placebo.
- 40% of patients were receiving ART at admission and median CD4 cell count 20 cells/ul

Outcomes

- Fungal clearance in cerebrospinal fluid was slower in the dexamethasone group
- Dexamethasone associated with more disability and AEs and the trial was stopped early.

<table>
<thead>
<tr>
<th></th>
<th>“Good” outcome (lack disability)</th>
<th>10 week Mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dexamethasone</td>
<td>13%</td>
<td>47%</td>
</tr>
<tr>
<td>Placebo</td>
<td>25% (P&lt;0.001)</td>
<td>41% (P=0.20)</td>
</tr>
</tbody>
</table>

Beardsley et al NEJM 16
OPENING PRESSURE MANAGEMENT

Opening pressure

- 50% patients > 250 mm H2O
- But most patients do not undergo therapeutic lumbar punctures despite reduction in mortality by 50%
  - COAT trial substudy:
    - No therapeutic LP: mortality 18%
    - Therapeutic LP performed: mortality 7%
    - Adj. risk of mortality with therapeutic LP 0.31
- Recommended: Daily LP if > 250 mm H2O and removal of up to 25cc until pressure <200 mm
- No significant risk of herniation; the problem is not edema and shift but obstruction of outflow
- In absence of manometry, recommend qd LP until symptoms well controlled.

JAIDS & Hum Retrovirol. 1998
CID 2014; 4: 59 (11)
Tuberculosis meningitis updates
Empirical treatment in HIV based on suspicion:

- CSF:
  - Lymphocyte pleocytosis
  - Depressed glucose, elevated protein
  - Negative CrAg and cryptococcal culture
  - TB evident elsewhere (i.e. CXR or smear)

Therapy:
- RHZE for 2 months, RH for 4-7 months further + corticosteroids for first 4-6 weeks

TB-M is a grave diagnosis for which we have weak diagnostic and treatment strategies.
In a UK study, the retrospectively evaluated CSF specimens known to be culture positive with the XPERT MTB/RIF assay.

The quantity of CSF available was small.

Overall sensitivity was 55% but specificity very high (few false positives).

- Sensitivity may as high as 72% with large CSF volume 10ml + centrifuge (Uganda, 2015).

When positive, XPERT MTB/RIF CSF testing can “rule-in” TB-M – and identify drug-resistant TB – but a negative test does not exclude TB-M when suspicion is high.

UK Retrospective Study

<table>
<thead>
<tr>
<th>Xpert MTB/RIF result</th>
<th>No. of samples</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Culture positive</td>
</tr>
<tr>
<td>Positive</td>
<td>25</td>
</tr>
<tr>
<td>Negative</td>
<td>20</td>
</tr>
<tr>
<td>Total</td>
<td>45</td>
</tr>
</tbody>
</table>

Role of adding levofloxacin + hi dose rif?

- Trial of TB meningitis in Vietnam (42% HIV-infected, median CD4 38)
- No advantage of adding – to RIPE and dexamethasone– levofloxacin and high dose rifampin during first 8 weeks

Role of linezolid?

- Small (n=33) study showed more rapid improvement of GCS, fever, and CSF parameters when linezolid 1200 mg/day added to standard regimen
- No mortality data provided. Larger trial needed.

Sun et al AAC 2014
NEJM 2016; 374:124-34
TB updates
TB DIAGNOSTICS IN ADVANCED HIV

- It is difficult to diagnose TB in inpatients with advanced HIV however post mortem studies show that many with HIV still die with TB.
- Alere Determine TB Ag lateral flow strip test is a bedside diagnostic using 60 ul of urine to detect lipoarabinomannan (LAM), a cell wall Ag.
  - It is most sensitive at CD4 count <200 cells/ul.
  - At <200 cells/ul = 50% sensitivity, 90% specificity.
- HIV-infected TB suspected admitted to hospital.
- In treatment arm, LAM added to routine TB work-up (smear, Xpert-MTB/RIF, and culture).
- By end of hospital day 1, in LAM group 55% started TB therapy vs 40% in no LAM group.

Peter J et al. Lancet 2015

Mortality improved by ~4% with LAM (8 w mort. 25% vs 21%)

Adjustment HR 0.82 (95% CI 0.70-0.96; p=0.015)

Effect size by country of implementation:

<table>
<thead>
<tr>
<th>Country of enrolment</th>
<th>No LAM</th>
<th>LAM</th>
</tr>
</thead>
<tbody>
<tr>
<td>South Africa</td>
<td>0.93</td>
<td>1.03</td>
</tr>
<tr>
<td>Tanzania</td>
<td>0.86</td>
<td>0.86</td>
</tr>
<tr>
<td>Zambia</td>
<td>0.66</td>
<td>0.66</td>
</tr>
<tr>
<td>Zimbabwe</td>
<td>0.87</td>
<td>0.87</td>
</tr>
</tbody>
</table>
RAFA: ART WITH STANDARD- VS HIGH-DOSE RIFAMPICIN IN HIV/TB-COINFECTED PTS

- Multicenter, open-label, randomized phase III trial
- Pts in Benin, Guinea, and Senegal
- Primary outcome: mortality at 12 mos post-randomization

ART-naive HIV/TB-coinfected adults with CD4+ cell count ≥ 50 cells/mm³ (N = 778)

- High-Dose Rifampicin, * Start ART at Wk 8 (n = 258)
- Standard-Dose Rifampicin, † Start ART at Wk 8 (n = 258)
- Standard-Dose Rifampicin, † Start ART at Wk 2 (n = 262)

*Rifampicin 15 mg/kg plus ethambutol, isoniazid, pyrazinamide.
†Rifampicin 10 mg/kg plus ethambutol, isoniazid, pyrazinamide.
ART regimen: EFV 600 mg + 2 NRTIs.

Pactr.org. PACTR201105000291300. EDCTP Project Portfolio.
RAFA: SURVIVAL OUTCOMES WITH HIGH- VS STANDARD-DOSE RIFAMPICIN

- Overall survival not improved, but high-dose rifampicin may benefit severely immunocompromised pts

<table>
<thead>
<tr>
<th>Overall Survival, %</th>
<th>HD RIF, ART Wk 8 (n = 249)</th>
<th>SD RIF, ART Wk 8 (n = 247)</th>
<th>SD RIF, ART Wk 2 (n = 251)</th>
</tr>
</thead>
<tbody>
<tr>
<td>12 mos</td>
<td>90</td>
<td>86</td>
<td>89</td>
</tr>
<tr>
<td>18 mos</td>
<td>90</td>
<td>85</td>
<td>88</td>
</tr>
</tbody>
</table>

Mortality for Pts With CD4+ Cell Count < 100 cells/mm³ (n = 159)

- HD RIF vs SD RIF, ART Wk 2: HR: 0.20 (95% CI: 0.04-0.90)
- HD RIF vs SD RIF, ART Wk 8: HR: 0.12 (95% CI: 0.03-0.55)

Bacterial pneumonia updates
WHAT IS THE MOST COMMON CAUSE OF BACTERIAL PNEUMONIA IN HIV?

1. *Streptococcus pneumoniae*
2. *Staph. aureus*
3. *Pseudomonas aeruginosa*
PROSPECTIVE STUDY OF PNEUMONIA IN HIV-INFECTED PATIENTS ADMITTED IN MALAWI

- HIV-infected patients with pneumonia and symptoms of <14 days prospectively enrolled
- Patients underwent a protocolized work-up
- Median CD4 ~100 cells/μl

The top 3 etiologies were *S. pneumoniae* (19%), *M. tuberculosis* (25%) and influenza (9%). Coinfection was common.

- 2/3 are potentially vaccine preventable
- *M. tuberculosis* is an important cause of acute presentations and linked with incr. 30 d mortality
- Patients with *S pneumoniae* or influenza had low mortality

CROI 2015 Aston et. al.
DISTINGUISHING BACTERIAL PNEUMONIA

Features favoring bacterial pneumonia:

• Leukocytosis
  • Most patients have leukocytosis or relative leukocytosis

• Lobar or segmental infiltrates most common
  • Hilar or other LAN uncommon
  • Bilateral infiltrates with reduced O2 saturation occurs but less common

• AFB, XPERT MTB/RIF and urine LAM negative

If no response in 48 hours, consider:

• Patient not receiving drug
• Coinfection such as TB, PCP, or fungi
• Infected collection (e.g. empyema)
• Antibiotic resistant or difficult bug (e.g. MRSA, ESBL-producer, Pseud.)
• Non infectious (e.g lymphoma or KS, VTE)
MANAGEMENT OF COMMUNITY ACQUIRED PNEUMONIA:
A BETA-LACTAM ALONE?

Guidelines have for years recommended a beta-lactam + macrolide (BLM) or fluoroquinolone (FQ) based on limited data.

In the Netherlands a trial compared: (1) beta-lactam monotherapy (2) BLM and (2) FQ for non ICU patients admitted with pneumonia.

Crude mortality for 90 days of follow-up:
- Beta-lactam monotherapy 9%
- Beta-lactam + macrolide 11.1%
- FQ 8.8%

Results indicated non-inferiority at 3% margin.

But nearly 40% of patients in the beta-lactam monotherapy group received coverage for atypical organisms during hospital period.

**Management initially?**
- Beta-lactam +/- macrolide
  - Ex. ceftriaxone 2 g/day +/- azithromycin 500 mg/day
- Avoid FQs given potential for misleading initial improvement in TB and risk for acquired resistance (10%)
- If PCP is considered: combination of beta-lactam PLUS high dose TMP-SMX PLUS corticosteroids reasonable
- If neutropenia or very severe pneumonia, coverage for *Pseudomonas* +/- MRSA reasonable

Postma D et al NEJM 2015
TRIAGE AND MANAGEMENT

- Most patients with HIV and pneumonia should be admitted, especially in presence of abnormal vitals or hypoxemia.
- Validated prediction tools for HIV patients admitted with LRTI in developing countries lacking
- Role for procalcitonin? May be a strong independent predictor of inpatient mortality in HIV
  - In Uganda, admitted HIV patients (N=241, median CD4 47) underwent smear, x-ray and if initial tests (-), bronchoscopy
  - Final diagnoses: TB 72%, bacterial pneumonia 12%, fungal pneumonia or PCP 6%, pulmonary KS 3%

<table>
<thead>
<tr>
<th>Oxygen saturation &lt;90%</th>
<th>Respiratory rate ≥30 breaths/minute</th>
<th>Procalcitonin ≤0.5ng/ml</th>
<th>Procalcitonin &gt;0.5ng/ml</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>No</td>
<td>No</td>
<td>1% (0.3–6)</td>
<td>10% (6–17)</td>
<td>0.004</td>
</tr>
<tr>
<td>Yes</td>
<td>No</td>
<td>4% (1–19)</td>
<td>26% (11–49)</td>
<td>0.32</td>
</tr>
<tr>
<td>No</td>
<td>Yes</td>
<td>3% (1–13)</td>
<td>19% (10–33)</td>
<td>0.25</td>
</tr>
<tr>
<td>Yes</td>
<td>Yes</td>
<td>9% (2–30)</td>
<td>42% (24–62)</td>
<td>0.17</td>
</tr>
</tbody>
</table>
ART INITIATION IN THE HOSPITAL
ART IN ADVANCED HIV
PRACTICAL FACTORS TO CONSIDER

• Drug-drug interactions between OI treatment and ART
  • Particularly with boosted PIs
  • Univ. of Liverpool has nice interaction algorithm: http://www.hiv-druginteractions.org

• Ability to swallow pills
  • There are few fully liquid regimens however potential options exist
  • See Univ. of Liverpool web site for dosing liquid formul. dosing in adults

• Renal impairment
  • Patients with renal impairment at increased risk for TDF-induced nephrotoxicity.

• Attributing causation when adverse events arise
  • Ex. A patient receiving RIPE for TB develops hepatitis after ART initiation (EFV-TDF-FTC)
  • Ex. A patient receiving high dose TMP-SMX develops rash after ART initiation (EFV-TDF-FTC)
### TIMING OF ART AFTER OI

There is some clear guidance from randomized trials:

<table>
<thead>
<tr>
<th>Condition</th>
<th>When to start ART?</th>
</tr>
</thead>
<tbody>
<tr>
<td>TB (non CNS) in patients with CD4&lt; 50 cells/ul *</td>
<td>Within 2 weeks</td>
</tr>
<tr>
<td>PCP,* bacterial pneumonia</td>
<td>Within 2 weeks or in ICU</td>
</tr>
<tr>
<td>OI with no effective specific therapy (Ex. chronic diarrhea)</td>
<td>Within 2 weeks</td>
</tr>
<tr>
<td>Lymphoma or KS anticipating chemotherapy</td>
<td>Within 2 weeks</td>
</tr>
<tr>
<td>TB in patients with CD4&gt; 50 cells/ul*</td>
<td>Within 4 weeks</td>
</tr>
</tbody>
</table>

**CNS OIs**

<table>
<thead>
<tr>
<th>Condition</th>
<th>When to start ART?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cryptococcal meningitis *</td>
<td>Defer until 5 weeks</td>
</tr>
<tr>
<td>TB meningitis</td>
<td>Unknown, consider defer until 5 wks</td>
</tr>
</tbody>
</table>
Consecutive ART naïve HIV-infected patients discharged after OI prospectively followed.

The median CD4 cell count was 42 cells/ul.

Prevalent OIs:
- Extrapulm. TB (38%)
- Pulmonary TB (28%)
- Pneumocystis pneumonia (8%)
- Chronic diarrhea (8%)
- Crypto. meningitis (6%)
- Toxoplasmosis gondii (4%)
- Other/unknown (8%)

Results:
- ART initiation by 6 months associated with less advanced HIV infection;
- CD4 < 50 associated with not initiating ART within 6 months of discharge.
WHAT HAPPENED TO HIV PATIENTS AFTER ACUTE OI IN 2007?

Trajectory After Discharge, McCord Hospital, Durban

- 41% Initiated ART
- 29% Died Prior to ART
- 9% Lost to follow-up or unknown

*6 month post-hospital mortality as high as 40%*

Discharge to ART: median 82 days
Discharge to death: median 95 days

Sunpath H et al Int J TB Lung 2011
Follow-up of hospitalized HIV patients recruited day 4

Most common condition was newly diagnosed TB
- 15% had a neurological diagnosis most often TB-M or CM
- Clinical deterioration on or AE to TB therapy also common

45% were receiving ART at admission

About 15% had a new HIV diagnosis; median CD4 cell count in this group was 123 cells/ul

6 m mortality: CF Jooste 18%

Mortality RFs: low Hb, reduced GFR and OI other than TB – especially neurological diagnosis

Patients admitted with HIV and concurrent TB or other OI initiated on early inpatient ART (N=382).

- 48% women with median CD4 count 33 cells/ul
- The median time from admission to ART start was 14 days (range 4–32, IQR 11–18)

Outcomes:

At 24 weeks of follow-up:
- Virol. suppression 93% with median change in CD4 count of +100 cells/ul
- Overall 24-week mort. was 25% with 5% LTFU
- Risk factors for mortality: >21 day delay prior to ART and age > 40 years

WHAT IS MOST EFFECTIVE INITIAL ART FOR PATIENT WITH RECENT OI WITH CD4<200 AND VIRAL LOAD > 100,000 COPIES?

1. Boosted-PI regimen
2. NNRTI-based regimen
3. Triple NRTI regimen
Clinicians commonly reach for boosted protease inhibitor-based regimens in advanced HIV.

What is actual data?

- ART naïve CD4 < 200 randomized to AZT/3TC + LPV/r or EFV
- Median CD4 64 cells/ul, VL > 75,000 in majority
- If OI present, ART initiated after OI therapy. TB patients excluded.
- At week 48, 70% of EFV and 53% of LPV/r patients achieved <50 copies/mL (P = 0.013)

Sierra-Madero J et al JAIDS 2010
OI prophylaxis updates
Prospective, randomized trial conducted in Zimbabwe, Malawi, Uganda, and Kenya

Primary endpoint: mortality at 24 wks

Enhanced prophylaxis: STD + fluconazole 100 mg/day, azithromycin 500 mg/day x 5 days, albendazole x 1

Additional randomizations conducted in factorial fashion*

*Raltegravir added to ART for 12 wks; food supplementation for 12 wks.
†Cotrimoxazole, isoniazid/vitamin B6 300/25 mg/day for 12 wks (IPT), fluconazole 100 mg/day for 12 wks, azithromycin 500 mg/day for 5 days, albendazole 400 mg (single dose).
‡Cotrimoxazole, IPT added after 12 wks (except in Malawi).
In both prophylaxis regimens, cotrimoxazole and IPT given at half doses if younger than 12 yrs of age.

Slide credit: clinicaloptions.com
### REALITY: MORTALITY BENEFIT WITH ENHANCED OI PROPHYLAXIS FOR Pts INITIATING ART

<table>
<thead>
<tr>
<th>Deaths, %(^1)</th>
<th>Enhanced Prophylaxis (n = 906)</th>
<th>Standard Prophylaxis (n = 899)</th>
<th>HR (95% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wk 24*</td>
<td>8.9</td>
<td>12.2</td>
<td>0.73</td>
<td>.03</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>(0.54-0.97)</td>
<td></td>
</tr>
<tr>
<td>Wk 48</td>
<td>11.0</td>
<td>14.4</td>
<td>0.75</td>
<td>.04</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>(0.58-0.98)</td>
<td></td>
</tr>
</tbody>
</table>

*Primary endpoint.

- 3.3 lives saved for every 100 treated with enhanced prophylaxis\(^1\)

PREVENTING PNEUMONIA

• Pneumococcal vaccination:
  • For vaccine-naïve patients:
    • Prevnar (PCV13) followed after 8 weeks by PPV23
  • For vaccine-experienced patients:
    • A single dose of Prevnar (PCV13) should be given ≥1 year after PPV23
• Influenza vaccination yearly
• TMP-SMX prophylaxis and ART also both reduce pneumonia risk considerably
TAKE - AWAYS

- We continue to see OIs as initial HIV presentation and in those lost from care
- PCP patients with resp failure have survival ~50% with mechanical ventilation and – if performance status good – should be offered intensive care
- For CM, consider fluconazole 800 mg/day as consolidation therapy
- For CM, ICP management with therapeutic LPs is essential
- TB-M still difficult to diagnose / treat but CSF XPERT a promising diagnostic
- Enhanced OI prophylaxis improves survival if starting ART with CD4<100
- Early ART – including ART prior to hospital discharge – should be considered in PCP, TB, bacterial pneumonia, and chronic diarrhea or in HIV-associated malignancies but not in CNS OIs.
- The first 6 months after discharge continues to be a very high risk period in SA
Thank you