Antiviral Therapy and Drug Resistance 20

Evolving Concepts in Antiviral Therapy & Drug Resistance

20th Annual Antiviral Therapy & Drug Resistance Meeting

Thursday 15 September 2016
WELLCOME COLLECTION, LONDON
Dr Margaret Portman
Mortimer Market Centre, London

<table>
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<tr>
<th>Speaker Name</th>
<th>Statement</th>
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<tr>
<td>Dr Margaret Portman</td>
<td>None Declared</td>
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<td>Date</td>
<td>September 2016</td>
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PrEP - Tackling Implementation

Dr Mags Portman
Mortimer Market Centre
15th September 2016
PrEP - Tackling Implementation

• UK HIV epidemiology
• PrEP “politics”
• Implementation – what is happening
• PrEP in your clinic
• Other considerations
1.5% of the population identifies as gay or lesbian (ONS & NATSAL)

2/3 of heterosexual people living in the UK with HIV are of black African ethnicity

Black African people make up 1.8% of the UK population
Incidence of HIV in MSM STI clinic attendees

Table 2. HIV incidence in HIV negative MSM who re-attended at STI clinics in 2012

<table>
<thead>
<tr>
<th>Category</th>
<th>HIV incidence (per 100 py)</th>
<th>95% CI</th>
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<tr>
<td>HIV test 42-365 days prior to current attendance</td>
<td>2.4</td>
<td>2.0-2.8</td>
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<tr>
<td>Diagnosed with bacterial STI in previous year and/or at current attendance</td>
<td>3.3</td>
<td>2.8-4.0</td>
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<tr>
<td>Diagnosed with rectal bacterial STI in previous year and/or at current attendance</td>
<td>5.2</td>
<td>3.7-6.7</td>
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<tr>
<td>Received post-exposure prophylaxis (PEP) in previous year</td>
<td>3.3</td>
<td>1.7-6.3</td>
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Source: GUMCAD, HIV & STI Department, Health Protection, PHE, HIV incidence analyses: 2012

Overall estimated incidence in MSM GUM attendees is 1.34
"NHS England is the responsible commissioner for all antiretroviral drugs (ARVs) including where they are used in HIV prevention either in preventing mother to child transmission or as post exposure prophylaxis following sexual or occupational exposure to HIV infection (PEP / PEPSE)"
NHSE – March 2016

• As set out in the Local Authorities (Public Health Functions and Entry to Premises by Local Healthwatch Representatives) Regulations 2013, local authorities are the responsible commissioner for HIV prevention services.

• Including PrEP for consideration in competition with specialised commissioning treatments as part of the annual CPAG prioritisation process could present risk of legal challenge from proponents of other ‘candidate’ treatments and interventions that could be displaced by PrEP if NHS England were to commission it.
Recent Developments

• Successful NAT legal challenge
  • NHSE *can* legally commission PrEP
  • NHSE plans to appeal
• PrEP back in the annual specialised commissioning prioritisation round
  • CPAG decision expected October 2016
• NICE evidence review underway
• Public Consultation underway
• NHSE has invited manufacturers of the drugs and treatments going to CPAG to submit “best and final prices”

Final funding decision lies with NHS England’s Specialised Commissioning Oversight Group, assured by the Specialised Services Commissioning Committee of the Board
European Commission Grants Marketing Authorization for Gilead’s Once-Daily Truvada® For Reducing the Risk of Sexually Acquired HIV-1

— Truvada is the first Antiretroviral Medicine to be Licensed in Europe for Pre-Exposure Prophylaxis, In Combination with Safer-Sex Practices, to Reduce the Risk of Sexually Acquired HIV-1 in Adults at High Risk —

FOSTER CITY, Calif.—(BUSINESS WIRE)—Aug. 22, 2016— Gilead Sciences, Inc. (Nasdaq: GILD) today announced that the European Commission has granted marketing authorization for once-daily Truvada® (emtricitabine 200 mg/tenofovir disoproxil FDC) in combination with safer sex practices to reduce the risk of sexually acquired HIV-1 infection among uninfected adults at high risk, a strategy known as pre-exposure prophylaxis, or PrEP. Truvada was approved by the European Medicines Agency in 2005 for use in combination with other antiretroviral agents for the treatment of HIV-1 infection in adults aged 18 years and over, and is currently the most prescribed antiretroviral medicine in Europe as part of combination therapy.

The marketing authorization allows for the marketing of Truvada for PrEP in all 28 countries of the European Union, subject to national regulatory authority approval of required pharmacovigilance materials in each country.
The 2 million

- NHSE agreed to fund £2million over 2y for PrEP
- Working with PHE to decide how this will be implemented via “early implementer sites”
- Unknown if will provide PrEP mainly for PROUD participants or "new" PrEP users
- Unknown what will happen to this process/funding if CPAG outcome is favourable
Proposed Criteria for Commissioning

• MSM, trans women and trans men*
  – *Intermittent regimen*
  – Daily regimen may be indicated (needs to be fully documented)

• Heterosexuals*
  – Daily regimen

*assessed as being at high risk of HIV acquisition
Assessment of “High Risk”

• MSM, trans women & trans men
  – Negative HIV test in past year
  – Condomless sex in past 3/12 & likely to continue
  – HIV+ partner not virally suppressed

• Heterosexuals
  – Condomless sex with HIV+ partner who is not virally suppressed w/i 3/12 & likely to occur again (with current or new partner)
Proposed Mechanism for Funding

- NHS England will reimburse the cost of antiretroviral drugs used for PrEP at specified providers (Level 3 GUM services) where the patient has been validated via a prior approval process and where data on outcomes is provided.

- Local authorities are the commissioners of sexual health services and will fund the service costs associated with PrEP.
  - Each local authority will be responsible for determining whether it will make access available.
Commissioner High Cost Drugs System

Take control of your PBRE High Cost Drugs budget:

- Collect the NICE criteria led evidence directly from the Provider Clinicians themselves.
- Using Auto-Approval, ensure that Clinicians receive the approval to treat immediately.
- Keep a complete audit trail of the process.
- Validate/Challenge provider invoices with ease.

Blueteq is delivering and enhancing IFR solutions that provide the flexibility and ease of use that the modern healthcare professional demands.
Grassroots Implementation
Where to get PrEP online

So far we have verified 3 different companies who sell the generic equivalent of Truvada which is produced by Gilead.

**United Pharmacies UK** (£44 per month)

United Pharmacies UK is our personally recommended supplier of PrEP. You do not need to upload a prescription after purchasing, and they have some of the cheapest prices on the internet. We have talked to one of their customers who uses them to get PrEP, who has also afterwards had the blood test which tests the amount of PrEP in your blood, and came back with perfect results. We have also used United Pharmacies to buy PrEP ourselves with no problems.

- 1 months supply = £45.79 per month
- 3 months supply = £126.07 in total
- Delivery to the UK costs £6.75 and takes 7 - 14 business days.
Generic PrEP monitoring
56 Dean Street

• 1\textsuperscript{st} February 2016 – started to formally offer monitoring for individuals taking, or intending to start taking generic PrEP within routine GUM service

• Patient information available in clinic and on 56 Dean Street PrEP clinic website [www.getprep.uk](http://www.getprep.uk) based on data from PROUD and Ipergay studies

• Obtained grant from St Stephen’s AIDS Trust to perform TDM

• Medical and nursing staff trained
Results

• 161 individuals seen

Of people with data available:

• 115/129 (90%) on daily PrEP
• 13/129 (10%) on event driven PrEP
• TDM performed in 125 individuals
Time-dependent concentration of plasma emtricitabine following generic oral PrEP consumption

Concentration of emtricitabine (ng/mL)

Time post-dose (hours)

- Sample generics pK
- Reference Truvada pK
- Predicted sample generics pK
- Predicted Truvada pK
Time-dependent concentration of plasma tenofovir following generic oral PrEP consumption

- Reference Truvada pK
- Sample generics pK
- Predicted Truvada pK
Hornet/ECDC survey on PrEP

PrEP (Pre-Exposure Prophylaxis) is a proven effective method to prevent HIV. It is becoming a popular option to help gay men take control of their sexual health. However, in Europe the approval of this drug is still behind other parts of the world. We are helping collect data to advocate for access to this HIV prevent tool and sharing these results at the request of the European Center for Disease Control. No personal information is collected and answers remain anonymous and are not connected to your Hornet profile in any way.
Hornet survey respondents

8543 persons responded between 23 – 25 April

26% France
22% United Kingdom (UK)
13% Russia
10% Italy
10% Germany
13% Turkey
10% Spain
10% Belgium
10% Netherlands
10% Denmark
10% Ukraine
10% Switzerland
10% Sweden
10% Portugal
10% Other
Are you currently taking PrEP?

n= 8048 (excludes HIV-positive respondents)

69% of those on PrEP said their sexual health provider was aware that they were taking PrEP.
Where did you obtain PrEP?

n= 528 persons on PrEP responding to this question

- **France**
- **Other**

<table>
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<tr>
<th>Source</th>
<th>Percentage</th>
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<tr>
<td>Research study</td>
<td>20%</td>
</tr>
<tr>
<td>Friend</td>
<td>10%</td>
</tr>
<tr>
<td>Internet</td>
<td>50%</td>
</tr>
<tr>
<td>PEP acquired and split</td>
<td>0%</td>
</tr>
<tr>
<td>Physician/doctor</td>
<td>20%</td>
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Other data

• iwantprepnow.co.uk
  – 12,000 new unique clicks through to website July/Aug 2016 compared with 6,000 the preceding month

• Grindr advert (24h, London only)
  – 311 respondents
  – 96% had heard of PrEP before
  – 7% taking PrEP (selection bias?)
  – low level of knowledge on where to source PrEP and the need to for monitoring
Self Sourcing of PrEP is happening!
Mortimer Market

• Offer of PrEP monitoring since end Jan 2016
• Patients attending routine GUM appointments
• Assessment and testing mainly via Band 5/6 nurses with senior support
• Electronic proforma
• Follow up of results and problems by telephone
Mortimer Market

- First 48 notes analysed (Jan-June 2016)
- 44% not started PrEP
- 19/44 Current drug use (43%)
  - 15/44 Current chem use (34%)
- 15/47 STI (32%)
  - 3/15 had 2 STIs
  - Mainly rectal infection
- >90% daily dosing – all thought around 100% adherence
- >90% generics
- 41% had eGFR <90
MMC - New Model

• Access for renal monitoring alongside STI screening remains
  – FU of results and issues via electronic worklist

• HIV/STI prevention clinic
  – Mainly in house referral for individuals identified as high risk and interested in PrEP
  – Those attending for monitoring who have not yet started PrEP
GMC letter

• “Doctors should give patients the information they want & need about options for treating & managing their condition, the potential benefits, burdens and risks for each option, & any treatments that they think have greater potential benefit for the patient than they or their organisation can offer. ... should read the GMC guidance on investigations and treatment"

• Important to document the discussion of risks and benefits
Your Clinic

• Do you actively discuss PrEP?
• Can you offer renal monitoring?
• Are you in touch with your local HIV prevention 3rd Sector organisation?
• Have you had any PrEP educational events?
Materials available

• BHIVA/BASHH PrEP Position statement
• Practical PrEP guide
• I-base PrEP guide
Key Points

• In someone at ongoing risk, do not delay PrEP, but ensure tests happen as they start

• If self sourcing, check what they are taking
  – (TDF *plus* FTC)

• Check *they* know what they are taking & how to take it

• Extra care in the first 4 weeks after starting*

• Extra care if a break in PrEP*

• Discuss other HIV & STI prevention methods and harm reduction

*Risk of drug resistance if HIV infection missed
eGFR 60-90

- Repeat creatinine or renal function
- Ensure urinalysis result available
- If eGFR remains 60-90 do Cockcroft Gault
- Medical assessment

Assess risk vs benefit ratio - likely can start PrEP
- Suggest 3 monthly creatinine plus urinalysis
PrEP after PEP

• No need to wait for 8 week HIV test
• Advise start straight onto PrEP after PEP
• Carry out additional HIV Ab/Ag test at PEP completion (4 weeks)
• If very high risk prior to PEP consider pro viral HIV DNA test (discuss locally with virology)
When to use PEP

• In reality, few people taking PrEP present for PEP
• There is no 'schedule' stating when PEP is indicated
• Individual assessment and discussion
Other Considerations

- Event-based dosing not recommended
  - Women (lower TDF concentrations in vagina)
  - Hepatitis B (potential for liver flare)

- Renal
  - More care needed if age >40y and/or eGFR <90 at baseline

- Young People
  - Bones
  - Adherence

Hosek, ATN 113 AIDS 2016
Mulligan, Bone changes in young men PrEP EACS 2015
Themed Discussion: It's Complicated: Renal Function in PrEP Users CROI 2016
Challenges

• Inequity of PrEP education, access and provision likely to remain with or without a national programme

• Nationally agreed funding for treatment does not automatically mean LA will fund a PrEP service

• Continuing need to re-educate & challenge misconceptions

• Initiating intermittent rather than daily regimen
San Francisco

Figure 1.2 New HIV diagnoses\(^1\), deaths, and prevalence, 2006-2015, San Francisco

1 See Technical Notes “Date of Initial HIV Diagnosis.”
Acknowledgements

• My colleagues at MMC
• Sheena McCormack
• Nneka Nwokolo, Marta Boffito, Tara Suchak
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Thank You

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