HIVPA STUDY DAYS

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TRIAL SUMMARY

A SUMMARY OF THE TRIAL DATA FOR THE NEWLY LI-CENSED JULUCA

HIVPA NEWS

LATEST UPDATES FROM THE COMMITTEE

HIVPA

HIV Pharmacy Association

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HIVPA News

Hello and welcome to the HIVPA bulletin! Thank you so much to all the authors for their valued contributions to this edition of the bulletin, as always it is greatly appreciated. If you would like to make a contribution to the February 2019 bulletin, we would be really excited to hear from you. Perhaps you have attended a study day or conference which you would like to share some valued learning from, or you may have enjoyed recent success with a local project or initiative– please do get in touch with the HIVPA committee via hivpaoffice@gmail.com. Unfortunately I will now be stepping down from my role as HIVPA Bulletin lead as I commence maternity leave shortly. I have thoroughly enjoyed the challenge of the role and would like to thank all the other committee members, whom I have had the pleasure of working with, for their time and support over the past three years. Our new bulletin lead, Bronagh McBrien, is based at Manchester University NHS Foundation Trust, I wish Bronagh every success and look forward to reading the next edition!

Thank you, and I hope you enjoy this issue,

Alli Lenko (HIVPA Bulletin Lead)

GDPR COMMUNICATIONS General Data Protection Regulation (GDPR) came into effect on 25/05/18. Our privacy policy has been updated in line with this new legislation, which we use your data in compliance with and reflects the new and strengthened rights in relation to data and how it is used. Our privacy policy can be found on www.HIVPA.org under the terms and conditions link. Members can unsubscribe to email communication at any time by clicking the 'Unsubscribe' link at the bottom of any email we send you. If you have any questions about the changes please email hivpaoffice@gmail.com and we will respond to you directly.

SPONSORS HIVPA would like to thank all of our sponsors for their continued support in 2018:

Gilead Sciences (UK) Ltd
Janssen—Cilag
Merck Sharpe and Dohme
Mylan
ViiV Healthcare
Dr. Reddy's Laboratories (UK) Ltd

The support of our sponsors is essential to much of the work carried out by HIVPA including events like our study days and conference. Thank you!

BURSARY AWARDS We are delighted to announce that in collaboration with Gilead, we have made provision, for a second year, for bursary awards to be made available to assist pharmacists and pharmacy technicians to attend conferences in 2019. There will be two awards:

The HIVPA Pharmacist of the Year Award
The HIVPA Rising Star Award

We would like to encourage applications from all members, irrespective of grade or experience. Please do not hesitate to contact us if you have any queries that cannot be answered with the supporting information previously sent by the committee on email. All application forms must be returned to corporate@hivpa.org, the deadline for applications is August 10th 2018.

HIVPA COMMITTEE Please welcome our newest committee members! Nipur Siani is joining the committee in the communications and e-learning role from Lloyds Pharmacy. Nipur has worked extensively on the collaboration with the HIV team at Imperial to provide the successful outpatient service to their cohort. Richard Strang from University Hospitals of Leicester is joining us in the new RPS Faculty Liaison and Support role. You will recognise Richards name as a recent contributor to the HIVPA bulletin. And of course Bronagh McBrien taking over the HIVPA bulletin Lead position.

HIVPA Conference 2018

The 2018 HIVPA conference took place in Manchester in June. This years conference committee did an absolutely fantastic job organising the event, which was a huge success. A special thank you to Lucy, Marina, Yvonne and Celesta for all their hard work! We would like to share a message sent to us from Professor Rob Miller (one of this years prestigious speakers) thanking the conference committee for all their hard work:

Belatedly – I'm writing to thank you for organizing the HIVPA Conference so well. As you can imagine, I am asked to speak at a variety of meetings – both in UK, and abroad. It is a rare pleasure to be invited to speak at a meeting that is superbly organised. The information prior to the meeting was timely, the onsite logistics (registration, delegate pack, room allocation, catering) were spot on, and the paperwork re expenses easily dealt with.
*A **BIG** thank you from me*

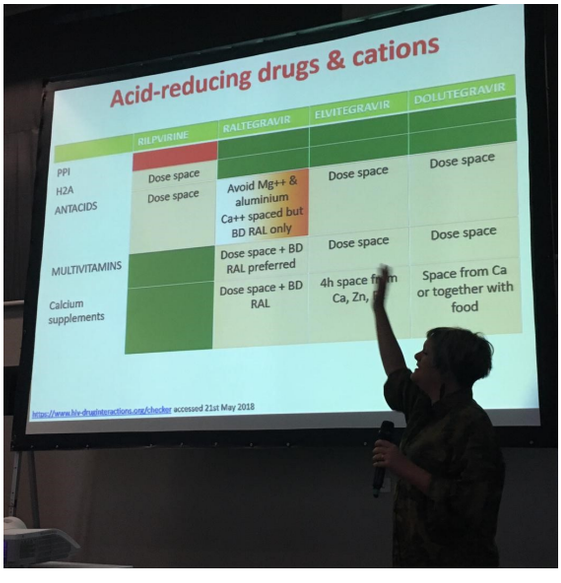
VBW
*Rob (**Professor RF Miller)***

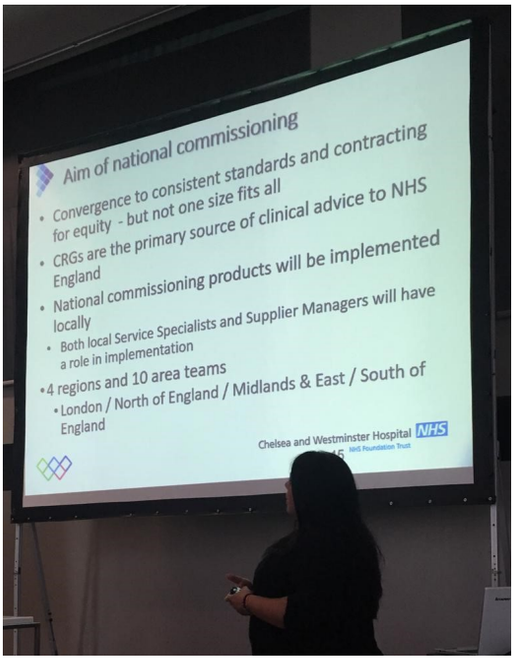
Poster Prizes

The 'Ushma Patel Memorial Poster Prize' 2018 were awarded to Jill Ross from County Durham and Darlington NHS Foundation Trust (1st prize) and to Sacha Pires from Brighton and Hove. Congratulations again to both!

HIVPA pharmacy technician membership donations

Sam Quaye from CPPE donated three free HIVPA pharmacy technician memberships in place of their speaker fee. We would like to say a big thank you to Sam for this generous donation. HIVPA has offered a further eight free places to those pharmacy technicians who applied for the initial free paces but were not successful. Welcome to our new pharmacy technician members!





HIVPA Conference 2018

After attending the HIVPA conference on Friday 15th June 2018, I am already excited for next year. The conference catered for those of all knowledge levels with a range of diverse and engaging talks, starting with the HIVPA committee chair outlining the learning events and opportunities that would occur throughout the year.

Starting the sequence of speakers was Dr Scott Murray – a consultant who specialises in cardiovascular disease (CVD). During the talk Dr Murray outlined the pathophysiology of CVD and how this is affected by HIV. With an ever aging population for our HIV cohort this talk was exceptionally relevant to everyone's practice! He summarised how ART can increase CVD risk and how to manage this – including when it is appropriate to use statins and a summary of the various methods to calculate cardiovascular risk, such as QRISK score and other risk measures such as JBS3.

The day was really thought provoking and diverse. Dr Mas Chaponda presented on clinical networks, which I have limited experience of, but I came away intrigued and full of ideas. In collaboration with a team of computer technicians and other healthcare professionals they developed an exceptional system for use in HIV clinics. By reviewing learning points from systems used for hepatitis C services and other areas he showed how you can develop relationships and networks to provide exceptional patient care.

Whilst all of the speakers were exceptional and I have several learning points from each; my personal highlight was a talk by Rebecca Tallon De Havilland from the Terence Higgins Trust. Her talk surrounding her experience of living with HIV and the stigma she has endured really made me take stock and critically review the way I practice. She explored the route of her distrust in medical professionals, stemming from damaging experiences during a time when treatment was limited, ART was toxic and life threatening and she was regularly losing friends around her, despite the best efforts of the HIV team. She explained how this impacted her relationship with her HIV team and her acceptance of treatment and still continues to do so. As someone who has only worked within HIV in the era of effective treatment, this was a completely different view to what I have experienced and it really showed me how patients need time and information. I also felt that her views on adverse drug reactions (ADRs) were very interesting; as healthcare professionals we can sometimes fail to understand how impactful a side effect may seem to someone who is experiencing it every day. It can act as a constant reminder of a condition that they may not yet have accepted or one they feel stigmatised by. Particularly those that have a physically visible impact, such as lipodystrophy, and how this may lead to patients not wanting to take their therapy. It's very easy to rationalise as a health care professional, with our knowledge of the medications and condition and assume that patients would accept something perceivably minor rather than have uncontrolled HIV, forgetting the complex psychology associated with managing a long-term condition.

Following such a heart wrenching presentation, which left barely a dry eye in the room, we ended the programme with a fantastic and informative quiz. Two senior pharmacists, Adele Torkington and David Ogden, and two physicians, Dr. Mas Chaponda and Professor Robert Miller, went head to head in a battle of wits and minds lead by quiz master Dr. Laura Waters. This was an hilarious as well as educational experience and a fantastic finish day one of conference!

SAVE THE DATE- HIVPA Conference 2019 will be held at the Crowne Plaza Hotel in Manchester on the 14th and 15th of June.

Feedback by **Emma Carter** University College London Hospitals NHS Foundation Trust

BHIVA/BASHH Fourth Joint Conference Feedback

Close to a 1000 delegates attended the 4th national joint BHIVA/BASHH conference in Edinburgh. A range of clinicians, scientists, public health experts, patient advocates and industry representatives came together to highlight and discuss current issues and advances in HIV and sexual health care. The four day conference consisted of seminars, workshops, lectures on updates to national guidelines as well as sharing results from audit and research projects conducted at a local level. 445 abstracts were submitted at conference; 45 oral and 400 poster presentations.

A range of themes were discussed at the conference from the management of vulnerable adults living with HIV, updates on various BHIVA and BASHH guidelines including gonorrhoea, mycoplasma genitalium, managing HIV infection in pregnant women, as well as regional updates on pre-exposure prophylaxis (PrEP).

Topics discussed during the lunchtime workshops included safeguarding in HIV and sexual health, recent developments in bacterial vaginosis, a review of the use of protease inhibitors and clinical cases on integrase inhibitors and interactions. Workshops were popular with delegates and well attended.

There were many excellent posters at the conference, all poster abstracts are available for review on the BHIVA website.

A selection of the posters I found interesting are listed below and worth a read:

⇒ A phase 3b open-label pilot study to evaluate switching to elvitegravir/cobicistat/emtricitabine/tenofovir alafenamide (E/C/F/TAF) single tablet regimen (STR) in virologically suppressed HIV-1 infected adults harbouring the NRTI resistance mutation M184V and/or M184I.

⇒ Ritonavir/cobicistat interaction with glucocorticoids: are simple preventative measures effective?

⇒ Dual therapy with dolutegravir and renally adjusted lamivudine in HIV infection: a treat ment strategy to manage comorbidity and toxicity in older patients

My personal highlights from conference were the following:

A brief update on managing intravenous drug users in HIV care by Dr Emma Thompson from the University of Glasgow. The presentation included details of the services developed to deal with an HIV outbreak amongst people who inject drugs in Glasgow. There have now been over 100 cases investigated with genetic sequencing showing that all cases were linked, with many of these infections involving HIV subtype C. Clade C of virus is rare amongst people who inject drugs in the UK. All cases originated in Scotland and through genetic resistance testing, two HIV mutations have been identified: V179E, associated with resistance to efavirenz, etravirine and nevirapine and E138A which is associated with reduced susceptibility to etravirine and rilpivirine. “The Scottish outbreak is being managed through education of the population at risk and service providers, improved addiction services, increasing provision of needle exchange (eg, greater evening availability), improving accessibility of HIV testing, and outreach services to support early treatment and retention,” conclude the authors. “Further research is needed to demonstrate whether homelessness, or other behavioural factors, played a role in the outbreak.”

An emotional and thought provoking series of talks on healthcare access for refugees and migrants were presented by Dr Fionnuala Finnerty and Dr Yusef Azad. Both speakers explored the problems facing this particularly vulnerable group of patients accessing HIV, TB and GUM care, examples demonstrated barriers to care provision such as healthcare charging and immigration detention.

An audit of perinatally acquired HIV in UK-born infants reported between 2014 to 2017 was presented by Ms Helen Peters from the University

BHIVA/BASHH Fourth Joint Conference Feedback

College London. Main findings were a decline in the number of perinatal transmissions over the period, two thirds of children were born to women undiagnosed by the time of delivery and over half of mothers experienced adverse social circumstances. The main issues identified in this audit were engagement with care services, late booking, declined HIV testing and seroconversion following an HIV negative test result.

Mr James McVeigh from Liverpool John Moores University gave an informative and captivating talk on the use of steroid supplements amongst the HIV positive MSM population. The take home message from this talk was the difficulty in safely advising on the use of any supplements due to the potential lack of strict quality assurance checks during production.

Attending my first BHIVA/BASHH joint conference was a great opportunity for me to network, see what clinical work is being done at local centres, hear talks given by leading experts in the fields of HIV and GUM and have the opportunity to ask questions. Conference has inspired me to participate in clinical audits and put forward my own abstracts for posters and perhaps even an oral presentation! I would strongly recommend when and where possible all HIV and sexual health pharmacists and technicians take the opportunity to attend conference, sharing their work and experiences with like-minded professionals. I look forward to seeing more pharmacy professionals at future conferences!

Nazlee Payghamy-Ashnai Imperial College Healthcare NHS Trust

HIVPA Regional Representatives

HIVPA have a team of Regional Representatives, led by Regional Lead, Portia Jackson, covering the whole of UK and who serve as the regional voices of the organisation. They support and communicate with HIVPA members in their region and look to provide networking and educational opportunities. They are your local point of contact with HIVPA .

Scotland:	Elspeth Boxall
	Kirsteen Hill
Wales:	Fiona Clark
North of England:	Kathryn Ashton
	Jill Ross
East and West Midlands:	Joanne Dey
	Alison Darley
South East Coast and London:	Stephanie Tyler
East Anglia:	Portia Jackson
South Central and South West:	Suzanne Elvin
	Denise Reeves
	Kerry Street
Northern Ireland:	Paul Rafferty

Should you wish to get in touch with your Regional Representative for any reason, for example if you have any questions or issues you would like raising with the HIVPA Committee, or have any suggestions for HIVPA, please email: hivpaoffice@gmail.com and your message will be forwarded to the relevant Representative(s).

-Portia Jackson

JULUCA

For over 20 years combination antiretroviral therapy (cART) with a 3 drug regimen has been the mainstay of HIV management in treatment naïve and virologically suppressed HIV-1 positive patients. However, the advent of the first licensed 2 drug regimen (2DR) may be set to significantly change the approach we take to managing 'stable' patients living with HIV.

Viiv has collaborated with Janssen-Cilag to produce Juluca, the first single-pill 2DR containing dolutegravir and rilpivirine which was licensed following promising trial outcomes from the SWORD-1 and SWORD-2 studies. The European AIDS clinical society (EACS) guidelines 2017 have already included dolutegravir/rilpivirine (DTG/RPV) as a recommended dual therapy in patients who are virologically suppressed and where a class-sparing strategy may be of clinical benefit. Although Juluca is the first licensed dual therapy it's not the only one recommended by EACS for use in clinical practice. The DUAL trial and SALT trials have already shown that lamivudine, in combination with darunavir/ritonavir or atazanavir/ritonavir respectively, is non-inferior to triple therapy in maintaining virological suppression. These trials were relatively small though and maintaining a PI-based regimen has the intrinsic downside of long-term lipid abnormalities and other metabolic disturbances despite avoiding NRTI-related toxicities.

This article will review the week 48 data from the SWORD-1 and SWORD-2 studies to interpret the potential benefits of a 2-DR which is NNRTI and PI -sparing while highlighting some of the clinical considerations for deciding who can be appropriately switched to Juluca.

SWORD-1 and SWORD-2 are identical open-label, randomised studies including 1,014 HIV positive patients who were stable on their current ART regimen (CAR) containing an NRTI backbone and a standard third drug (NNRTI, PI or INSTI). These phase 3, multicentre, parallel-group trials will run alongside each other across 12 countries for a total of 148 weeks. Participants were included if they were over 18 years of age, were on their first or second ART regimen and were virologically suppressed for a minimum of 6 months. Participants were excluded if they had significant resistance mutations related to the main drug classes (NRTIs, NNRTIs, PIs and INSTIs), hepatitis B co-infection, substantial suicidality risk (determined subjectively by the investigators), a corrected QT (cQT) of 450ms or longer, or were pregnant or breastfeeding. While it seems reasonable to exclude people at high risk of QT prolongation if being prescribed rilpivirine it's noteworthy that this group excluded those at highest risk of suicide where dolutegravir is considered likely to exacerbate psychiatric issues; more on this later.

In terms of pertinent demographics, the average age of each group was 43 years old, predominantly white (82% DTG/RPV vs 78% CAR) and male (77% DTG/RPV vs 79% CAR). Considering patients were on their first or second ART regimen without significant mutations and fully suppressed (VL<50 copies/mL at baseline) with an average duration on CAR of 4.25 years, baseline CD4 counts were high (611 cells/mL vs 638 cells/mL CAR) as would be expected and the patients generally well; 11% of patients in each group had been diagnosed with an AIDs defining illness at baseline.

A larger trial size than has been seen in previous

dual therapy trials allowed a conservative non-inferiority margin of 8% when results from each study were pooled while also accounting for confounding by third-agent and age (<50 years and ≥ 50 years). To give some context, the majority of patients (54%) in each treatment group were on an NNRTI as their third drug, presumably most people were on efavirenz previously as only 10% of patients had previously been on DTG or RPV; of the remainder 26% vs 27% were on a PI (most commonly DRV/r) while 20% vs 19% were on an INSTI (most commonly RLG) for the DTG/RPV and CAR groups respectively. A large proportion of patients were on tenofovir (73% vs 70%) and emtricitabine (69% vs 67%) as part of a Truvada back bone with a large number of people presumably on Atripla; this allowed for a substudy on bone mineral density (BMD) with people switching away from TDF.

Pooled analysis of the intention-to-treat population saw DTG/RPV meet it's primary endpoint of maintained viral suppression (<50 copies/mL) at week 48 after switching from CAR; 95% maintained viral suppression in each group, adjusted treatment difference -0.2% (95% CI -3.0 to 2.5). The number of patients not achieving viral suppression was low, approximately 1% across each group, while the remaining 4% were not included in the 48 week analysis due to a lack of data; this is a common occurrence with intention-to-treat analysis and how 'failures' are reported. Of the three virological failures in the DTG/RPV group there was only 1 NNRTI mutation (K101K/E) and no integrase-associated mutations.

Improvement in CD4 count was consistent across all sub-groups for each arm but relatively modest (28 cells/mL vs 22 cells/mL) although not particularly surprising considering the high baseline values. Although there was no particular benefit to switching in regards to immune function there was no disadvantage of being on a 2DR either.

Adverse events, if patients reported one event by week 48, were fairly similar amongst groups (77% DTG/RPV vs 71% CAR) which may be considered surprising as many patients were stable on CAR for over 4 years. Grade 1 events occurred equally in 48% of each group while grade 2 (23% vs 20%) and grade 3 (5% vs 3%) events were more common when switching to the study drug as may realistically be expected (where 87% of patients were new to DTG and RPV). Adverse events leading to withdrawal were more significant with DTG/RPV than with CAR which suggests that not everyone is likely to benefit when switching from a stable regimen. Adverse neuropsychiatric events related to study drugs were more common in the DTG/RPV arm (5% vs <1%); insomnia (3% vs 2%), depression (3% vs 1%) and abnormal dreams (1% vs 0%) although anxiety was comparable with 2% of people affected in each arm. Headache and diarrhoea occurred at equal frequency and were more commonly associated with DTG/RPV (2% vs 1%).

Total psychiatric adverse events, related to the study drug or not, were reported in 12% of switch patients compared to 6% on CAR. Although researchers did not attribute all incidents to study drugs there was no explanation as to why psychiatric issues may be twice as frequent in the DTG/RPV arm. Many people switched from an EFV containing regimen so, due to the long half-life of EFV, there may be some overlap of side effect profiles with DTG. However, incidents occurred gradually more frequently as the study progressed which would not fully explain this observation and suggests dolutegravir isn't always suitable for patients with previous psychiatric side effects or relevant previous medical history.

JULUCA

Although no difference was seen between serum fasting lipid, inflammatory or cardiovascular biomarkers between groups there was a statistically significant improvement in bone-turnover biomarkers and BMD in the Dexa sub-study (n= 102). The BMD sub-study saw a 1.29% and 1.32% improvement in hip and lumbar spine BMD respectively compared with those continuing on TDF-based regimens. This may be of particular relevance for patients who cannot simply be switched to an abacavir-containing regimen due to cardiovascular risk and are ineligible for TAF.

Overall, a large number of people were successfully switched to DTG/RPV while maintaining viral suppression with minimal incidence of virological failure and no significant mutations. Some key considerations when prescribing Juluca is that the SWORD cohort generally demonstrated good adherence prior to enrolment and were carefully screened for previous suicide risk. Where many patients were switched off an EFV containing regimen and still experienced DTG related neuropsychiatric effects it is important to consider the clinical significance of this in practice and review CNS side effects regularly if switching, as this could impact compliance and quality of life. Where patients may not fully appreciate the benefits of reducing the number of ARVs they are taking there is a role for patient education while the small pill size will be amenable to many. Patients with previous adherence concerns or interacting medications, particularly PPIs and potent enzyme inducers, shouldn't be considered appropriate for dual therapy owing to the low genetic barrier associated with rilpivirine where this 2DR could be considered particularly fragile.

While the prescribing guidance for Juluca recommends dose separation with H2-antagonists and antacids it would be prudent to avoid Juluca in patients who cannot strictly adhere to these requirements. Although further data from the SWORD trials will be essential in determining how effective and tolerable this 2DR is in the long term, Juluca has obvious advantages in carefully selected patients.

Suggestions for further reading

https://clinicaltrials.gov/ct2/show/NCT02422797

https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(17)33095-7/fulltext

https://julucahcp.com/sword-1-and-2/

Trial summary and reflection by **Richard Strang**
University Hospitals of Leicester NHS Trust

HIVPA Study Days– To Sum It Up

HIVPA hold four study days during the year which are always popular with our members because we invite high profile speakers to address topical clinical issues. Here is a summary of the topics discussed at the most recent study days from the speakers themselves.

Remaining dates and topics for 2018

Research, cure, "How to": conduct critical appraisal, journal article review style session, fake news, advanced practice, posters **19th September 2018**

New treatment guidelines, resistance and switch **7th November 2018**

The study days are open to any pharmacy or healthcare staff especially those with a special interest in HIV, so please feel free to share information about these events with your colleagues. Attendance is free for HIVPA members. A small charge is required for non members, payable in advance.

The Study Days are held at the Pullman hotel, 100-110 Euston Road, London NW1 2AJ near Euston and Kings Cross train stations.

To reserve your space on any of our Study Days please email Yvonne on hivpaoffice@gmail.com

Recent feedback comments from study day attendees:

Very informative and highlights areas that may not be experienced in each clinic.

A very interesting and extremely informative meeting.

Very informative study day, lots of very useful information + some very impressive speakers. Starting later a good idea in terms of travel. Thanks!

Menopause and HIV

Almost two-thirds of women report symptoms during the menopause including hot flushes and mood changes, lasting a median of 7.4 years and often impacting upon women's quality of life.

Approximately 10,500 women of menopausal age (45-56 years) attended for HIV care in the UK in 2016, a fivefold increase since 2006. As life expectancy with HIV increases, age-related events such as menopause become increasingly important. Menopause in women living with HIV is relatively under-researched. The few studies that have been conducted have largely been in the US, where the cohort of women living with HIV is very different to that in the UK. Studies suggest that women living with HIV may experience menopause at an earlier age and have increased menopausal symptoms compared to their HIV-negative counterparts. Furthermore, women living with HIV are at increased risk of comorbid conditions such as cardiovascular disease and osteoporosis, compared to women without HIV.

As a response to the paucity of data on menopause and HIV in the UK, we set up the PRIME (Positive Transitions Through the Menopause) Study (www.ucl.ac.uk/prime-study). PRIME is a mixed methods observational study of nearly 900 women living with HIV aged 45-60 attending 21 HIV clinics across England. Our research question is: What is the impact of the menopause transition on the health and well-being of women living with HIV?

Key findings from PRIME so far include:

* GPs report low confidence in managing menopause in women living with HIV. Their concerns include drug-drug interactions and missing an HIV-related diagnosis.
* Women report being 'bounced' between GPs and HIV specialists when trying to address menopausal services.
* Women describe the challenges of having to manage menopausal symptoms when already living with HIV including distinguishing symptoms and adhering to antiretroviral therapy.
* PRIME Study participants report a high prevalence of symptoms: vasomotor symptoms (89%), psychological symptoms (78%), and urogenital symptoms (68%).
* Use of systemic hormone replacement therapy (HRT) and vaginal oestrogens is extremely low in this group (<10%).

A related analysis of data from the POPPY study (Pharmacokinetic and Clinical Observations in People Over Fifty, a cohort study of people ageing with HIV) has revealed that prevalence of cardiovascular risk factors are similar in women aged ≥50 with and without HIV. Both groups of women were undermanaged for hypertension and dyslipidaemia.

PRIME Study findings have helped inform new BHIVA/BASHH/FSRH guidelines on management of menopause in women living with HIV. Key recommendations are:

* To conduct annual review of menstrual cycle until a woman is assessed as being postmenopausal

* To assess menopausal symptoms assessment in women aged >45
* To discuss and offer HRT as per NICE guidelines
* To aim for management within primary care (with close liaison between HIV teams and GPs)
* To provide information about menopause to all women living with HIV
* To perform bone screening as per BHIVA monitoring guidelines

These guidelines are an important step towards maintaining the health and well-being of women living with HIV across the life course.

Dr Shema Tariq UCL Centre for Clinical Research in Infection and Sexual Health

Update on Contraception Guidelines

It has been a very rewarding though long (and still ongoing) journey being part of the writing committee for the guidelines with the longest name ever: **BHIVA/BASHH/FSRH guidelines for the sexual & reproductive health of people living with HIV.** And that is without writing out the abbreviations!!

The guidelines are a wonderful resource and cover a huge range of topics which was not possible to cover in a whole study day never mind just 30 minutes, hence I had to narrow down the key points….no mean feat!

The main updates and significant changes to the guidelines were in the sections below and I will briefly discuss some of the pharmacy relevant areas:

- Cervical Screening update
- Practical guidance regarding conception advice and fertility screening
- Undetectable=Uninfectious U=U
- Pre-exposure prophylaxis for conception
- Contraception considerations
- Menopause
- Intimate partner violence
- Sexual dysfunction

Fertility: The impact of suppressive ART on fertility is conflicting. Progression of HIV is associated with decreased pregnancy rates and live birth rates but data from US suggests lower likelihood of conception on ART but large African cohorts report higher pregnancy rates among women on ART [1,2]

Conception: Changes here reflect what is happening in the general treatment arena with the message to treat all and U=U so if the partner isn't on ART then they should be encouraged to start. If they are already on ART with a VL<50 for 6 months with high adherence, then conception can take place by normal means.

PrEP-C is not recommended for patients with VL<50 for over 6 months (and STIs are treated) as there is no evidence of added benefit but it can be considered if VL>50, case by case. Women wishing to conceive should start as per BHIVA guidelines with preferential selection of ARVs with Antiretroviral Pregnancy Registry data supporting safety. Sperm washing is listed as an option (if VL>50) but funding can be difficult.

Contraception

Over half the people living with HIV are women and rates of unplanned pregnancies are extremely high, particularly in adolescents and young women.

A case review in a London clinic of teenagers with HIV showed 82% of pregnancies were unplanned and 65% said they hadn't used any contraception[3], hence the role of contraception in addition to condom advice is of utmost importance particularly in the era of U=U where condom use is diminishing.

The guidelines are an adjunct to the Faculty of sexual and reproductive healthcare documents (FSRH) which provide evidence-based guidance on contraceptive methods. The FSRH guidance uses a tool called the UKMEC (the UK medical eligibility criteria) that classifies a range of medical conditions into eligibility categories by contraceptive type. The categories are listed in table 1. It is really important to note that this is based on safety, not efficacy, and this is particularly important when considering interactions with ARVs. Although an ARV may be safe with a contraceptive method, there may be an interaction that means it is not effective. The range of contraceptives and their effectiveness are shown in table 2.

Table 1: UKMEC ELIGIBILTY CRITERIA

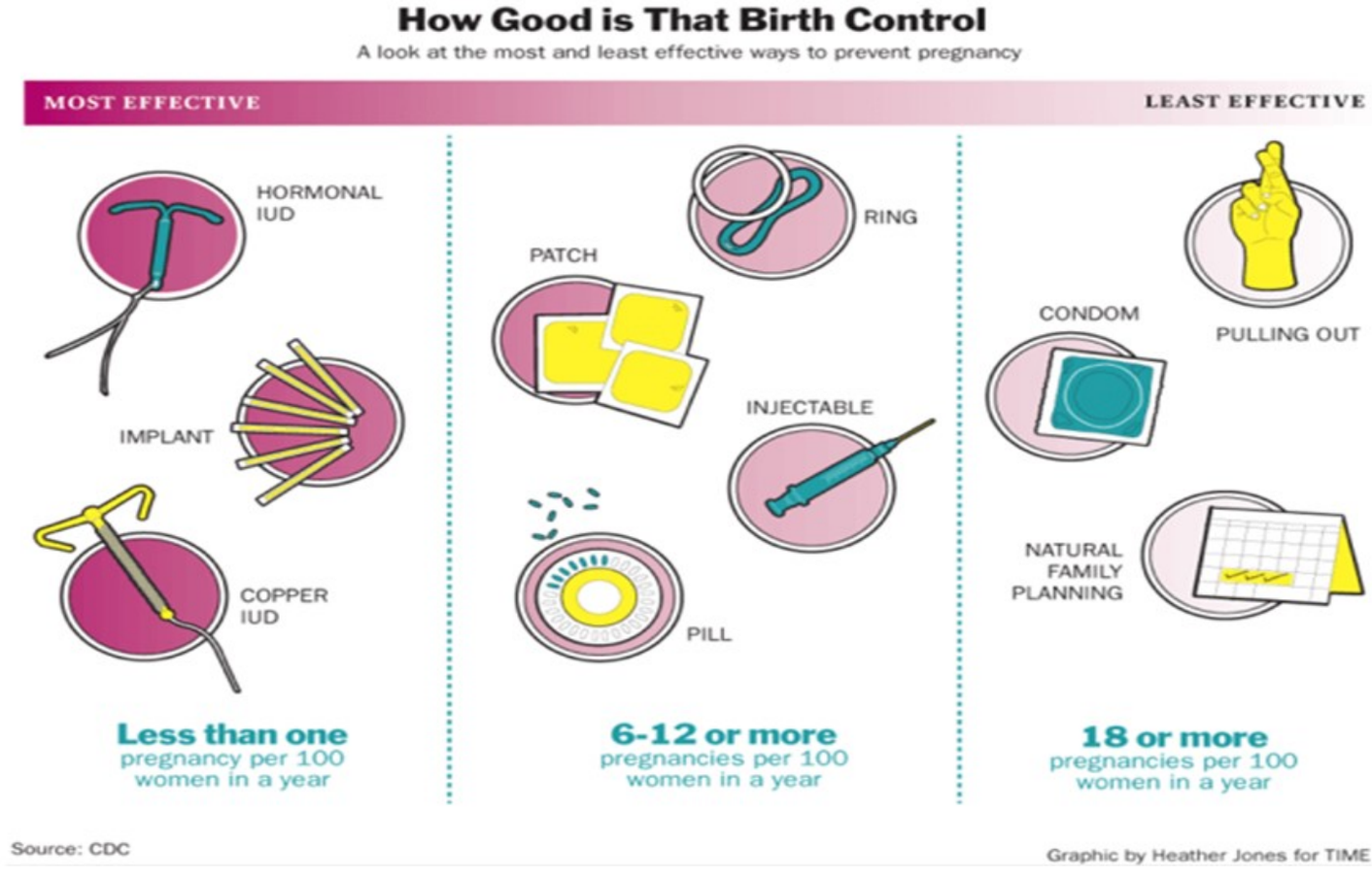
CATEGORY 1	**A condition for which there is no restriction for the use of the method**
CATEGORY 2	**A condition where the advantages of using the method generally outweigh the theoretical or proven risks**
CATEGORY 3	**A condition where the theoretical or proven risks generally outweigh the advantages of using the method.**
CATEGORY 4	**A condition which represents an unacceptable health risk if the contraceptive method is used**

The key points from the contraception section are:

- HIV infection is not a barrier to any form of contraception so WLWH (women living with HIV) should be given verbal and written information about all available contraceptive choices and a contraception history should be taken at every visit and any unlicensed use documented
- Most contraceptives can be used safely in WLWH but need to consider those with CD4<200 (for insertion of LNG-IUS and Cu-IUD) and those on ART for interactions
- Consistent condom use is advised in conjunction with an additional contraceptive method. Dual methods are recommended to prevent pregnancy and to reduce transmission, but may not be needed in the context of suppressive ART. Women using condoms alone should be aware of or be given emergency contraception
- If ART is a barrier to optimal contraceptive efficacy due to the impact of DDIs then ART may need to be switched (so long as there are reasonable alternatives)

- The efficacy of DMPA, LNG-IUS and Cu-IUD are largely unaffected by DDIs with ART and offer very effective contraception

Table 2:



Points of note:

Although the progestogen only implant (DMPA) is one of the most effective forms of contraception it is not recommended for use with Efavirenz due to decreased drug concentrations over time and many reported failures.4 This is given a UKMEC category 1 because it is safe but it is not effective!

There continues to be evidence of a possible increased risk of acquiring HIV among progestogen-only injectable users. Uncertainty exists about whether this is due to methodological issues or a real biological effect. In many settings, unintended pregnancies and/or pregnancy related morbidity and mortality are common, and progestogen-only injectables are among the few types of methods widely available, hence the consensus is that women should not be denied this form of contraceptive but should be advised about these concerns, about the uncertainty over whether there is a causal relationship, and about how to minimise their risk of acquiring HIV. Obviously if the person is already HIV positive then it is OK to use progestogen only injectables taking into account concerns around BMD, especially in young and older patients.

HIVPA Study Days– To Sum It Up

Interactions

⇒ Most of the hormonal contraceptives, both oral and systemic are metabolised via the cytochrome P450 isoenzyme system and by the glucuronidation pathway, and as they have a have a narrow therapeutic range an increase in clearance may lead to decreased contraceptive efficacy

⇒ Ethinyl estradiol (EE) is predominantly metabolised by CYP3A4 and CYP2C9 (minor CYP 2C19) and via glucuronidation by the uridine 5-diphosphate glucuronosyltransferase (UGT) isoenzymes particularly UGT1A

⇒ Most progestogens are metabolised by the CYP3A4 isoenzyme although there is a lot of inter and intra-individual variability

⇒ The exceptions to the limitations posed by drug-drug interactions are DMPA and the LNG-IUS (and the barrier methods) which to date have had no major interactions reported with any of the ARVs. Although DMPA is a substrate of CYP3A4, its clearance is approximately equal to the rate of hepatic blood flow so it is unlikely that enzyme inducing drugs will significantly affect levels of DMPA

⇒ NRTIs are renally cleared so there are no expected interactions with any contraceptives

⇒ Conversely some NNRTIs, PIs and Elvitegravir/cobicistat may increase clearance of hormonal contraceptives. The effect is not fully understood but does involve induction of glucuronidation and probably induction of CYP2C9, CYP1A2 & CYP3A4

⇒ Nevirapine is an inducer of CYP3A4, and therefore would be expected to lower levels of EE and progestogen, which has been shown in older studies. But a recent study from Malawi has demonstrated increased concentrations of both EE and progestogen and another study has shown no differences in ovulation or pregnancy rates so maybe advice for nevirapine will change in the future

⇒ Thankfully, a lot of the newer ARVs do not use these metabolic pathways (or use to a lesser extent) hence they can be used safely, increasing the contraceptive options available to women on ARVs

⇒ The newer NNRTIs etravirine and rilpivirine appear not to cause any significant alterations in EE and progestogen levels despite etravirine being a weak CYP3A4 inducer and weak CYP2C9 inhibitor

⇒ Maraviroc has no effect on CYP inhibition and has only a weak inducing effect on CYP2D6, hence does not affect EE or progestogen metabolism and studies have shown it is safe for co-administration with hormonal contraceptives

⇒ Interactions with PIs are complicated by the boosters ritonavir and cobicistat (to a lesser extent) and the PI itself

⇒ The PIs, darunavir, and lopinavir when boosted with ritonavir, result in significantly lower levels of EE and sometimes lower levels of progestogen and hence are not recommended to be used with hormonal contraceptives (except DMPA and LNG-IUS)

⇒ The effects of the newer booster cobicistat is largely unknown, but it would be expected to result in different interactions as it does not induce the CYP450 isoenzymes nor glucuronidation, but it acts as a potent CYP3A4 inhibitor and weak CYP2D6 inhibitor so levels of the hormones will be

determined by the concomitant PI

⇒ Atazanavir boosted with ritonavir behaves differently as atazanavir on its own is an inhibitor of UGT which counters some of ritonavirs induction effect. This results in only slight reductions in EE levels, and the progestogen levels remain high. Studies have indicated that boosted atazanavir can be used with the oral combined contraceptive pill that contains doses of at least 30 µg of oestrogen and the progestogen, norgestimate

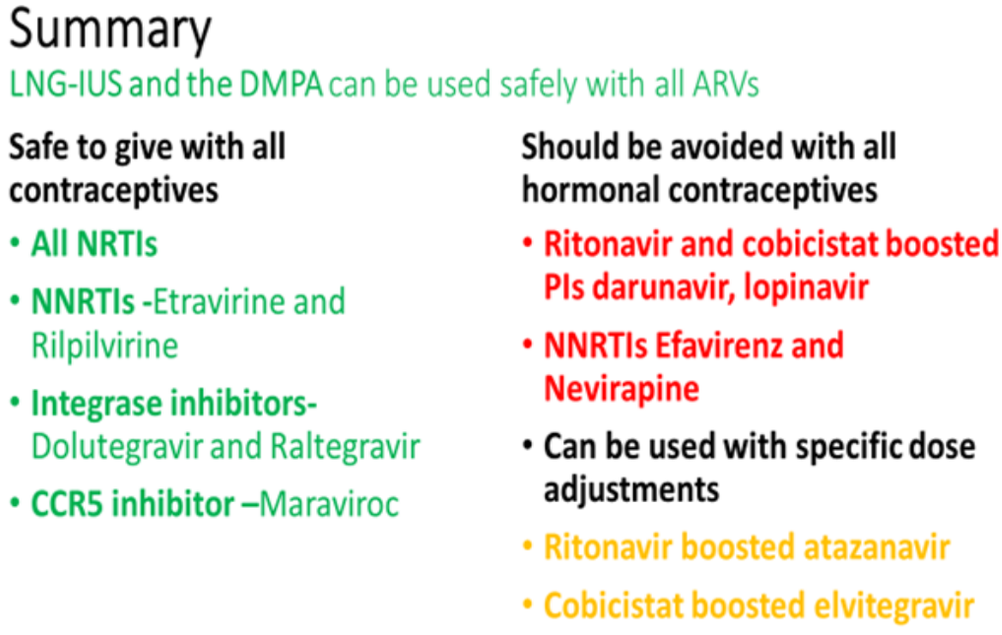
⇒ There is no data on cobicistat boosted atazanavir but it is expected to produce higher levels of progestogen, so would need to consider thrombosis risk etc

⇒ Raltegravir and dolutegravir, are well known for their lack of DDIs and do not affect the pharmacokinetics of EE or progestogen, therefore both are safe to use with all hormonal contraceptives

⇒ Elvitegravir has a different pharmacokinetic profile as it is boosted with cobicistat, and is itself a modest inducer of CYP2C9 and UGT. Boosted elvitegravir, lowers EE levels and raises progestogen levels but this can be compensated by increasing the EE. The data suggests it can be given with an oral contraceptive that has at least 30 µg of oestrogen and norgestimate as the progestogen

Emergency Hormonal Contraceptive

Current FSRH guidance recommends that women using liver enzyme inducers should be advised to use a Cu-IUD. If progestogen-only EC is to be used it should be given as soon as possible and within 72 hours of UPSI. In women using liver enzyme inducing drugs, two 1.5 mg LNG tablets should be taken (3 mg) as a single dose- but efavirenz is the only inducer that significantly affects levels!! Hence the other ARVs are OK to use with standard dose of LNG. Ulipristal data is very lacking, but as it is metabolised by CYP3A4 you should avoid using with efavirenz, nevirapine and etravirine. But PIs and elvitegravir/cobicistat are ok as a single dose (i:e short term inhibition of CYP3 A4 enzyme) won't lead to any serious effects.



HIVPA Study Days– To Sum It Up

References:

1: Massad LS et al. Pregnancy rates and predictors of conception, miscarriage and abortion in US women with HIV. AIDS 2004 Jan 23;18(2):281-6

2: Myer L et al. Impact of antiretrovial therapy on incidence of pregnancy among HIV-infected women in Sub-Saharan Africa: a cohort study. PLos Med 2010;9;7(2):e1000229

3: Elgalib A, Hegazi A, et al. Pregnancy in HIV-infected teenagers in London. HIV Med. 2011 Feb;12 (2):118-23

4: Scarsi K et al. Efavirenz- but not nevirapine decreases exposure of levonorgestrel released from a subdermal contraceptive implant HIV Drug Therapy Glasgow Nov 2014

Antiretroviral Drug	Recommendation for Combined Hormonal (pills, patch, ring) contraceptives	Recommendation for DMPA	Recommendation for progestogen implant and POP	Recommendation for LNG-IUS and Copper IUD	Recommendation for Emergency Contraception with Levonorgestrel	Recommendation for Emergency Contraception with Ulipristal
NNRTIs						
Efavirenz	Alternative/additional methods	No impact on efficacy expected	Alternative/additional methods	No impact on efficacy expected	Copper IUD or double dose (3mg) Levonorgestrel	Copper IUD
Nevirapine	Alternative/additional methods	No impact on efficacy expected	No impact on efficacy expected	No impact on efficacy expected	No impact on efficacy expected	Copper IUD
Etravirine	No impact on efficacy expected	No impact on efficacy expected	No impact on efficacy expected	No impact on efficacy expected	No impact on efficacy expected	Copper IUD
Rilpivirine	No impact on efficacy expected	No impact on efficacy expected	No impact on efficacy expected	No impact on efficacy expected	No impact on efficacy expected	No impact on efficacy expected
PIs						
Atazanavir/r	For the COC can use when dose of EE=30ug with norgestimate as the progestogen. Not advised with other hormonal methods as not studied.	No impact on efficacy expected	No impact on efficacy expected	No impact on efficacy expected	No impact on efficacy expected	No impact on efficacy expected
Darunavir/r	Alternative/additional methods	No impact on efficacy expected	No impact on efficacy expected	No impact on efficacy expected	No impact on efficacy expected	No impact on efficacy expected
Lopinavir/r	Alternative/additional methods	No impact on efficacy expected	No impact on efficacy expected	No impact on efficacy expected	No impact on efficacy expected	No impact on efficacy expected
INIs						
Raltegravir	No impact on efficacy expected	No impact on efficacy expected	No impact on efficacy expected	No impact on efficacy expected	No impact on efficacy expected	No impact on efficacy expected
Dolutegravir	No impact on efficacy expected	No impact on efficacy expected	No impact on efficacy expected	No impact on efficacy expected	No impact on efficacy expected	No impact on efficacy expected
Elvitegravir/cobi	For the COC can use when dose of EE=30ug with norgestimate as progestogen. Not advised with other hormonal methods as not studied.	No impact on efficacy expected	No impact on efficacy expected	No impact on efficacy expected	No impact on efficacy expected	No impact on efficacy expected
CCR5 Inhibitor						
Maraviroc	No impact on efficacy expected	No impact on efficacy expected	No impact on efficacy expected	No impact on efficacy expected	No impact on efficacy expected	No impact on efficacy expected

Sharon Byrne HIVPA Expert Panel

HIVPA Study Days– To Sum It Up

The role of a specialist pharmacist in managing the care of the adolescent cohort

- Definitions of an "adolescent" vary – the current BNF definition is "from 12 years up to 18 years of age"
- We all know that children are not small adults so we must remember that adolescents are not the same as small children
- It is important to acknowledge that available evidence indicates that a significant proportion of children with perinatally acquired HIV have long term neuro-developmental or neurocognitive difficulties severe enough to interfere with everyday functioning, including school performance
- 2133 patients have been reported to CHIPS (Collaborative HIV Paediatric Study) – a multicentre cohort study of HIV infected children in UK and Ireland established April 2000
- 932 (44%) young people have left paediatric HIV care to move to adult clinics. This means 50 – 120 patients transferring each year (2009 – 2016). Median age of transfer = 17 years
- A brief case study demonstrated how things can go well in even the seemingly most engaged of young people
- These days it is important to maintain an "open door" policy in clinic for young people. We can manage appointments in university holidays and work around their lives
- 35% of patients aged 15 years and above have been exposed to 8 or more antiretroviral drugs
- Licensing regulations for fixed dose and combination tablets vary – important for pharmacy staff to appreciate this
- The PENTA (Paediatric European Network for Treatment of AIDS) Treatment Guideline 2016 update is that antiretroviral therapy is recommended for all children living with HIV
- Options in PENTA Treatment guidelines were discussed – what to start
- Brief discussion regarding NHSE commissioning policies and whether these are relevant to adolescents
- Discussion around adherence in adolescents and demonstration of some useful adherence aids (dosette boxes, pill holder keyrings, pill swallowing cups, PillGlide spray, MEMScaps)
- CHIVA summer camp and Freedom To Be information presented together with some information on the young people's experiences https://www.youtube.com/watch?v=g6WaL7QfjnI https://www.youtube.com/watch?v=BAuKYZ2tSlE
- Finally a case study demonstrating success in an adolescent patient was presented.

Kate Gandhi Lead HIV Pharmacist, Birmingham Heartlands Hospital

Adolescents living with HIV

This short article summarises some of the issues faced by adolescents and young adults (AYA) living with HIV with an emphasis on outcomes for those infected perinatally living in the UK. For those requiring more detailed reading two recent journal special issues on the global picture for adolescents living with HIV are highly recommended: J Int AIDS Soc. 2017;20 Suppl S3 and Current Opinion in HIV and AIDS to be published May 2018.

Adolescents: definition

The World Health Organisation (WHO) defines adolescents as young people aged 10 to 19 years, young adults aged 20 to 24 years, with "youth" variably defined as 13-24 years or 15-24 years.[1] Whilst age definitions vary, there is increasing recognition that the biological, social and neurocognitive tasks of adolescence continue well into the third decade of life; reflected in the uniformity of 24 years as the upper age boundary. 1.8 billion young people, more than a quarter of the worlds population, are aged between 10 and 24 years, one fifth of whom live with a chronic health care problem originating in childhood. Adolescence is the period of developmental transition from childhood to adulthood and encompasses complex multisystem physical, neurocognitive and psychosocial change.

Epidemiology: HIV and adolescents

Adolescents are disproportionately affected by HIV, directly in terms of new infections and HIV associated mortality, and indirectly in terms of living in a family affected by HIV such as orphaned by parental loss and becoming young carers. In recent estimates 1.8 million adolescents were amongst the 36.7 million people living with HIV, 80% in sub-Saharan Africa.[2.3] Two main groups exist; those who have lived with HIV from early life, perinatally infected (PaHIV) and young people acquiring HIV during adolescence, the later accounting for 250,000 of the 2.1 million new HIV infections in 2015.[2] The success of antiretroviral therapy (ART) has changed the perinatal epidemic markedly; firstly in prevention of mother to child transmission and secondly paediatric antiretroviral therapy (ART) has resulted in increasing numbers of children surviving into adolescence to join their behaviourally infected (BHIV) peers, the majority acquiring HIV through unprotected sex.[2,3] Adolescent girls and young women in sub-Saharan Africa are disproportionately affected, accounting for 20% of all new diagnoses, though they represent just 11% of the population, with rates up to eight times that of their male peers reported in some countries.[4] Whilst recognising the global lack of robust data disaggregated by age and route of transmission, late adolescence (15-19 years) is the only age group in which deaths due to AIDS increased between 2005 and 2012; the majority thought to be the long term survivors of perinatal infection.[3]

Retention and Adherence in Adolescents: resourced settings

90:90:90 targets have yet to be met for adults in many well resourced settings and remain an enormous challenge for those caring for AYA living with HIV. The HIV care continuum for adults aged 15 years and over report highly variable retention and suppression rates. However encouragingly a recent report from Public Health England showed that in 2016 the 90:90:90 targets were met for the first time in London, with 97% of people diagnosed receiving treatment and 97% of those receiving treatment virally suppressed <200c/ml.[5] However when disaggregated by age, disparities persist with 89% of 15-24 year olds receiving treatment compared to 98% of those over 50 years. Disaggregation further by route of infection reveals those living with PaHIV have the lowest rate of viral suppression; 88% compared to 97%

overall, with injecting drug users of all ages achieving higher suppression rates.[6] In the US half of the 60,900 American youth living with HIV in 2013 remained undiagnosed, the highest rate in any age group. Of those diagnosed in 2014, 68% were linked to care within one month, the lowest of any age group, 55% were retained in care with 44% having a suppressed viral load.[6] More recently, specialist youth services with integrated mental health and substance use services have shown improvements in retention in care on sustained suppressive ART.[7] The global challenges of retention in care for this age group are recently reviewed by Enane et al but highlights the added complexities of maintaining suppressive ART during healthcare transition.[8]

Transition

Transition in adolescent healthcare is typically defined as "a purposeful, planned process that addresses the medical, psychosocial and educational/vocational needs of adolescents and young adults with chronic physical and medical conditions as they move from child-centered to adult-oriented health care systems." The period of transitional care is associated with poorer outcomes in many chronic diseases and in the context of HIV has recently been comprehensively reviewed.[9] However in summary, an effective transition process should be individually tailored to achieve the same goal; the supported provision of appropriate medical and psychosocial care for all young people growing up with a significant medical condition. Provision of HIV transitional services carries additional demands; not only must the young person achieve autonomy and learn to manage their own healthcare, they must appreciate how to safely negotiate disclosure of their HIV status and consider the implications and prevention of onward viral transmission as they become sexually active. These additional challenges, with the wider public health implications, underpin why provision of HIV transitional services must be well planned, supported by motivated adolescent focused multi-disciplinary teams.

UK outcomes

Children diagnosed with HIV in the UK and Ireland are followed prospectively in the Collaborative HIV Paediatric Study (CHIPS) cohort (http://www.chipscohort.ac.uk/), however currently data collection ceases on transfer to adult care, typically at 17-18 years of age. More than half of the 2100 children registered in CHIPS have now transferred to adult care (http://www.chipscohort.ac.uk/patients/summary-data/). By 2015, 291 of 644 UK adolescents transferring to adult care had failed treatment and had resistance data available; 82% had resistance to ≥1 drug class, 56% to ≥2 classes and 12% had triple-class resistance and reflect the long term consequence of paediatric viral suppression rates that fall below adults due to reduced paediatric ART options, unpalatable formulations, and a dependency on parents/carers.[10] Due to lack of robust national data following transfer to adult care, that will hopefully be addressed in the planned CHIPS+ cohort study, sparse data from single centres provides some information on outcomes in later adolescence. Retrospective cohort analysis of PaHIV AYA attending the 900 Clinic, a specialist service for young adults at Imperial College Healthcare NHS Trust in London between 2006 and 2017 showed excellent retention in care and low mortality but a fifth struggling with adherence and mental health issues. 182 PaHIV registered; 16 (8.7%) subsequently transferred care, 4 (2.2%) were lost to follow up (>12 months LTFU) and 4 (2.2%) died at a median age 20 years of end-stage HIV with poor ART adherence (3) and HIV/HBV hepatocellular carcinoma (1). Of 158 in current follow up, median age 22.9 years (range 18.1-33.6), 56% are female and 85% Black African ethnicity. Six (4%) have hepatitis co-infection. 157 (99.4%) have ever received ART; one age 19, CD4 336 cells/ul continues to decline therapy. At latest follow up 127/158 (80.4%) have a VL <200 c/ml, median CD4 count 626 cells/ul (IQR 441-820). 18 (11%), median 23.7 years, have severe immunosuppression, CD4 <200 cells/ul, 4 with suppressed viral loads.

128/158 (80%) are on standard ART; 2 NRTIs plus a; protease inhibitor (56%), integrase inhibitor (27%) and NNRTI (17%). 22 (14%) are on complex 3 ART class regimens, 50% VL <200 c/ml, median CD4 268 (IQR 54-670) cells/ul, half with prior mono/dual therapy, with dual (53%) triple (37%) and four class (10%) resistance mutations. Post transition, 14 (9%) had 1 or more new AIDS diagnoses: HIV wasting (4), recurrent sepsis (4), lymphoma (3), MAI (3), Cryptococcus (2), PCP (2) and MDR TB (1). Six had surgery for lipodystrophy and 6 gastrostomies for adherence. Co-morbidities: 13 (8%) have significant disability; 4 severe learning, 5 motor due to infantile HIV encephalopathy (4), anorexia (1) and sensory impairments of hearing (5) and vision (2). Mental health: 33 (21%) anxiety and/or depression of whom 3 attempted suicide and 4 self harmed, 8 (5.6%) new onset psychosis, and 6 (4%) alcohol/drug dependency. 13 women and 3 men are parents to 25 uninfected children.[11] Whilst larger cohort analyses are required, this data highlights the successes and complexities faced by adolescents and young adults living with HIV in the UK.

Specific ART considerations for Adolescents and Young Adults

AYA have lower rates of viral suppression on ART when compared to younger children or older adults. Robust, once daily low pill burden regimens are generally preferred. Rates of mental health issues are higher in AYA living with HIV when compared to general aged matched population data, although similar to their uninfected siblings.[12] Efavirenz based combinations should be used with caution, with consideration of 400mg dosing particularly for those in lower weight bands (40-50 kg) and high rates of switching off efavirenz based regimens are reported in UK paediatric cohorts.[13] Concerns over the emerging potential association of integrase inhibitors, particularly dolutegravir with potential neurotoxic side effects requires monitoring and further exploration within the AYA population.[14] Peak bone accrual occurs around 25 years of age, exposure to tenofovir disoproxil fumarate has been associated with reduced bone density and increased rates of renal toxicity in adolescents.[15,16] Tenofovir alafenamide (TAF) has an improved toxicity profile and the needs of adolescents during bone development is noted in the NHS commissioning statement;

“The HIV positive population most at risk include children and young people below the age of peak bone mass (aged approx. 25 years), those who have already had a low-trauma fracture, those who fall frequently, post-menopausal women and those on long term glucocorticoid therapy. These risk factors should be taken into account when considering TAF (category 2).” (https://www.england.nhs.uk/wp-content/uploads/2017/03/f03-taf-policy.pdf).

TAF is licensed from 12 years of age and 35kg and should be considered for AYA under 25 years for whom abacavir is not a suitable alternative. Drug-drug interactions are less frequent in AYA when compared to older adults due to reduced comorbidities and polypharmacy. However specific advice is required around contraception, including emergency contraception, iron and mineral supplements with integrase inhibitors, topical and systemic steroids with boosted regimens as well as recreational drug use.

In summary

The enormous success of suppressive antiretroviral therapy means increasing numbers of children born with HIV are surviving into adult life, negotiating education, employment and relationships and having healthy uninfected children of their own. However a proportion struggle with adherence and mental health issues and require adolescent friendly multidisciplinary support.

HIVPA Study Days– To Sum It Up

References

1. World Health Organisation. Adolescent Health. Available at www.who.int/topics/adolescent_health/en/ (Accessed July 2017).
2. UNAIDS. AIDSinfo [Internet]. 2015 [cited 2016 Aug 20]. Available from: http://aidsinfo.unaids.org/
3. Slogrove AL, Mahy M, Armstrong A, Davies MA. Living and dying to be counted: what we know about the global adolescent HIV epidemic. J Int AIDS Soc. 2017;20 Suppl 3:21520.
4. Kharsany ABM, Karim QA. HIV infection and AIDS in sub-Saharan Africa: Current status, challenges and opportunities. The Open AIDS Journal. 2016;10:34-48.
5. Towards elimination of HIV transmission, AIDS and HIV- related deaths in the UK; Update 3rd October 2017 https://www.gov.uk/government/news/phe-publishes-elimination-of-hiv-and-hiv-testing-reports-2017 (accessed 19th November 2017)
6. CDC HIV Surveillance reports; HIV among youth. https://www.cdc.gov/hiv/group/age/youth/index.html (accessed 19th November 2017).
7. Lally MA, van den Berg JJ, Westfall AO, Rudy BJ, Hosek SG, et al; Adolescent Medicine Trials Network for HIV/AIDS Interventions (ATN). HIV Continuum of Care for Youth in the United States. J Acquir Immune Defic Syndr. 2017 Oct 4. doi: 10.1097/QAI.0000000000001563. [Epub ahead of print]
8. Enane L, Foster C, Vreeman R. Retention and adherence: Global challenges for the long-term care of adolescents and young adults living with HIV. Curr Opin HIV and AIDS 2018 in press.
9. Foster C, Fidler S. Optimising HIV transition services for young adults. Curr Opin Infect Dis 2018; 31(1): 33-38.
10. Collins IJ, Foster C, Tostein A, Tookey P, Riordan A, Dunn D, Gibb DM, Judd A. Clinical status of adolescents with perinatal HIV at transfer to adult care in the UK/Ireland. *CID* 2017 15; 64(8): 1105-1112.
11. Foster C, Ayers S, McDonald S, Frize G, Fidler S. Post transition outcomes in young adults living with HIV: 90:99:80. BHIVA BASHH Edinburgh April 2018 (O4).
12. Vreeman RC, McCoy BM, Lee S. Mental health challenges among adolescents living with HIV. J Int AIDS Soc. 2017 May 16;20(Suppl 3):21497.
13. Wynberg E, Williams E, Tudor-Williams G, Lyall H, Foster C. Discontinuation of Efavirenz in Paediatric Patients: Why do Children Switch? Clin Drug Investig. 2017 Nov 27. doi: 10.1007/s40261-017-0605-1. [Epub ahead of print]
14. Elzi L, Erb S, Furrer H, Cavassini M, Calmy A, Vernazza P, Günthard H, Bernasconi E, Battegay M; Swiss HIV Cohort Study Group. Adverse events of raltegravir and dolutegravir. AIDS. 2017 Aug 24;31(13):1853-1858.
15. Sudjaritruk T, Bunupuradah T, Aurpibul L, Kosalaraksa P, Kurniati N, Sophonphan J, Ananworanich J, Puthanakit T; Bone-D study group. Impact of tenofovir disoproxil fumarate on bone metabolism and bone mass among perinatally HIV-infected Asian adolescents. Antivir Ther. 2017;22(6):471-479.
16. Lim Y, Lyall H, Foster C. Tenofovir-Associated Nephrotoxicity in Children with Perinatally-Acquired HIV Infection: A Single-Centre Cohort Study. Clin Drug Investig. 2015 May;35(5):327-33.

Caroline Foster Imperial College Healthcare NHS Trust

My Research Journey

I recently conducted a research project and have been asked to share my experience and learning.

The project was retrospective and aimed to evaluate the outcomes of NHS England scheme of switching PLWH from Atripla to Truvada and generic Efavirenz (gEFV). The project looked into tolerability of the switch, reasons for switching away from Atripla and reasons for subsequently switching off gEFV.

One concern was that a number of patients are now actively seeking a switch away from efavirenz, where previously they 'managed' with low-level, long-term side effects on efavirenz. This seems to be driven by increased awareness within the patient cohort that alternative drugs are available and that efavirenz is no longer considered a first line choice of therapy. Thus when approached regarding a switch in therapy, some patients have used this as an opportunity to discuss their treatment as a whole.

The results showed that majority of patients that switched to Truvada and gEFV stayed on this split regimen and tolerated this. This is reassuring in the current financial climate in the NHS where there is considerable pressure to switch to generics where possible.

The key reason for discontinuation with gEFV was found to be CNS toxicity. This is not a surprising adverse drug reaction of efavirenz. However, over half of patients that reported this felt it was due to the generic switch, which was a significant finding from this review. The difference in bioavailability of efavirenz between the various generic brands may have accounted for the increase in adverse effects seen post-switch in our patient cohort.

I found this particularly interesting as we assume that when switching patients to generics they will tolerate this and we reassure patients of this. However with this switch we found that a few patients had developed adverse effects.

In other specialities we routinely switch patients to generic medication and minimal counselling is given to the patient, whereas within the HIV speciality additional counselling and leaflets are routinely provided to patients. Prior to this switch, we have done this most recently, switching patients from Kivexa to its generic equivalent with very few reports of adverse effects reported.

Perhaps we may need to think about how we approach and manage patients who do develop adverse effects to generics.

From conducting this review, I have learnt the importance of having a good data collection tool. Investing time early to create the best data collection tool saves time later and helps with analysis of results.

I also did not anticipate the time required for data collection and the importance of allowing sufficient time for this, with realistic deadlines is helpful.

I thoroughly enjoyed conducting research and was lucky to have the time and opportunity to do this at CWH. With the large numbers of patients we have elicited some good results which I was able to present at the BHIVA annual conference and internally at our Trust research and development awards event.

Stephanie Tyler Chelsea and Westminster Hospital NHS Foundation Trust

A review of switching people living with HIV (PLWH) from Atripla to Truvada & generic efavirenz (gEFV).

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Chelsea and Westminster Hospital NHS
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Background

- NHS England introduced a Commissioning for Quality and Innovation (CQUIN) scheme, commencing December 2016, for HIV Service providers to switch patients on Atripla to the separate components Truvada and generic efavirenz. The scheme had a target of at least 60% of all patients to be switched.
- To meet the target all PLWH at CWH on Atripla were asked to switch their cART from Atripla to Truvada & gEFV. If a single tablet regimen (STR) was strictly required, an alternative STR was considered.
- The switch was discussed during their regular clinic visit, with counselling and written information provided by the pharmacist.
- One concern was that a number of patients are now actively seeking a switch away from efavirenz, where previously they 'managed' with low-level, long-term side effects on efavirenz. This seems to be driven by increased awareness within the patient cohort that alternative drugs are available and that efavirenz is no longer considered a first line choice of therapy. Thus when approached regarding a switch in therapy, some patients may use this as an opportunity to discuss their treatment as a whole.
- Another concern is that some patients after switching to gEFV and Truvada have experienced side effects and consequently been switched to a different anti-retroviral regimen entirely.
- Based on these concerns it was decided to review the impact of switching all patients.

Aims

To evaluate:

- Outcomes of NHSE switch scheme
- Tolerability of switch
- Reasons for switching away from Atripla
- Reasons for subsequently switching off gEFV

Method

- A list of all patients on Atripla on 1st April 2016 was used to identify PLWH on Atripla who formed the baseline cohort for the CQUIN.
- Electronic prescribing, dispensing systems and medical notes were retrospectively reviewed between October – December 2017 to identify PLWH switched to and away from Truvada & gEFV or to a different cART and reasons for switch.
- Demographic data was collected; time in months established on Atripla and ethnicity if EFV central nervous system (CNS) toxicity occurred.

Results

- From a total of 2547 patients on Atripla 1556/2547 (61%) switched to Truvada & gEFV and 48/2547 (2%) to different NRTIs & gEFV.

Figure 1: PLWH switch off Atripla

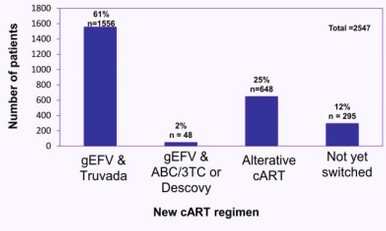
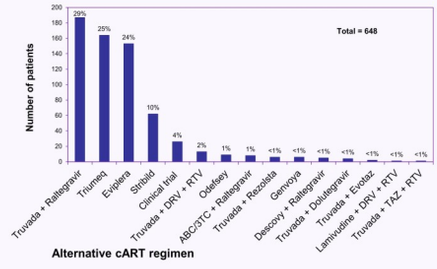


Table 1: PLWH not yet switched to gEFV & Truvada

Reason	N, (%)
Lost to follow up	138, (47%)
Transferred their care	88, (30%)
Not yet seen in clinic	61, (21%)
Enough supplies to delay switch	4, (1%)
RIP	4, (1%)
Total	295, (100%)

648/2547 (25%) patients switched to a different cART.

Figure 2: Atripla switch to alternative cART



- 1507/1604 (94%) remained on gEFV and 97/1604 (6%) subsequently switched off gEFV.

Figure 3: Indications for switch OFF gEFV

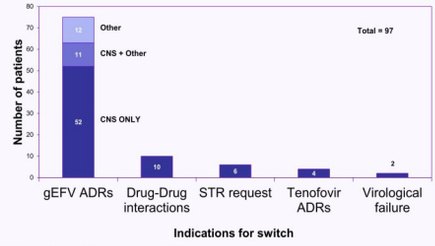


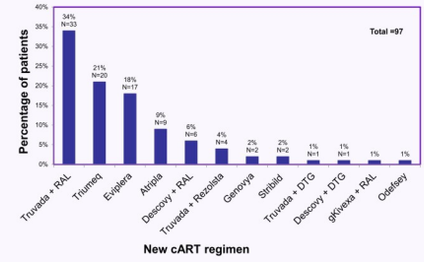
Table 2: ADRs to gEFV

gEFV ADR	Incidence (N)	gEFV ADR	Incidence (N)
Psychiatric disorders		Nervous system side effects	
Insomnia	23	Dizziness	6
Vivid dreams	18	Lack of concentration	4
Depression/low mood	17	Headache	4
Anxiety	6	Drowsiness	2
Night sweats	3	Grogginess	1
Hangover effect	2	Fatigue	1
Suicidal thoughts	2	CNS SE not specified	1
Memory problems	1	Bitter taste	1
Tingling sensation	1		
Metabolism and nutrition disorders		Gastrointestinal disorders	
Raised cholesterol	2	Nausea/ Vomiting	4
Raised lipids	1	Dry mouth	1
Low appetite	1	Diarrhoea	1
Low vitamin D	1		
Hepatobiliary disorders		Skin and subcutaneous tissue disorders	
Abnormal LFTs	3	Rash	1
Musculoskeletal disorders		Hypersensitivity disorders	
Aches/pains	3	Throat swelling	1
Other		Reproductive system and breast disorders	
Worsening Tourette's	1	Gynaecomastia	1

Note: some patients had more than one ADR to gEFV.

- CNS toxicity was the most common reason for discontinuation from gEFV - 63/97 (65%); of which 34/63 (54%) patients felt these had developed since switch to gEFV.
- 2 patients switched off gEFV due to virological failure because of non-adherence and resistance developed (M184I + K103N).
- 1507/1604 (94%) remained on gEFV and 97/1604 (6%) subsequently switched off gEFV.

Figure 4: PLWH that switched OFF gEFV



- Majority of PLWH who suffered ADR(s) to gEFV were of white British origin. Note: ethnicity was only recorded for PLWH who experienced an ADR.
- The cost implication of switching to an alternative regimen showed to be insignificant compared to the cost savings made by switch. The table below also does not account for cost implications of switching to TAF or resource cost of implementing the switch.

Table 3: Cost implication & savings from switch

Cost savings from switching Atripla to Truvada & gEFV	£1,190,340
Cost implication of switching to an alternative regimen	£314,227

Discussion

- Majority of patients (94%) that switched to gEFV remained on this regimen. This is reassuring in the current NHS financial climate with the need to make cost savings using generics.
- The key indication for discontinuation of gEFV was CNS toxicity.
- Bioequivalence studies for MHRA licensing purposes mean gEFV may have up to 20% lower or 20% higher levels in comparison to branded product. This small difference in the case of efavirenz may have contributed to the increased ADRs seen post-switch in our cohort.
- When Atripla therapy was reviewed a number of patients switched away from EFV or tenofovir disoproxil for clinical reasons. This highlights the importance of regular ART review.
- With imminent Atripla patent expiry there may be an opportunity to offer patients a return to an STR, however only a minority of patients switched off Atripla to another STR solely to avoid pill burden.
- The NHSE switch target was met and significant cost savings were generated as every patient seen was initially switched. Consideration should be given to achievability when targets are designed. It is important to ensure patients are engaged with any switch schemes.
- The results may be underestimated as data collection took place up until November 2017 and therefore there may still be some patients presenting to clinic post switch who have experienced ADR(s) to gEFV.

Dates for your diary

BHIVA Autumn Conference 4-5th October 2018, London www.bhiva.org

International Workshop on HIV & Ageing 13-14th September 2018, New York www.virology-education.org

HIV Glasgow 2018 28th-31st October 2018, Glasgow www.hivglasgow.org

UKCPA events 2018

13 Sep, London, e-Prescribing
25 Sep, London, Optimising medicines management in care homes
28 Sep, London, Critical Care advanced practitioner meeting
02 Oct, London, Medicines Optimisation Meeting (Cardiovascular)
05 Oct, Birmingham, Infection Masterclass
02 Nov, London, Pharmacy Together 2018 Conference
07 Dec, Merseyside, Starting out in critical care

http://ukclinicalpharmacy.org/education/events/

BHIVA World AIDS Day Event 30th November 2018 www.bhiva.org/world-AIDS-day-2018.aspx

UCL Research Methods: HIV, Sexual Health and Infectious Diseases 10-13th September 2018, Glasgow www.ucl.ac.uk/lifelearning/courses/research-methods-hiv-sexual-health-infectious-diseases

HIVPA
HIV Pharmacy Association

In the management of HIV,

TIMES ARE CHANGING

Are your treatment decisions changing with them?
Now is the time for a 2-drug regimen
for your suppressed patients.*

* JULUCA▼ is indicated for the treatment of HIV-1 infection in adults who are virologically suppressed (HIV-1 RNA <50 copies/mL) on a stable antiretroviral regimen for at least 6 months with no history of virological failure and no known or suspected resistance to any NNRTI or INI

Prescribing Information

Juluca▼ dolutegravir 50mg/rilpivirine25mg tablets
See Summary of Product Characteristics (SmPC) before prescribing **Indication:** Indication: HIV-1 in virologically suppressed adults (HIV-1 RNA <50 copies/mL) on stable ART for at least 6 months with no history of virological failure and no known resistance to any NNRTI or INI. Dosing: Adults (over 18 years): one tablet once daily with food. Elderly: Limited data in 65+ yrs. Caution in severe hepatic or renal impairment. Contraindications: Hypersensitivity to any ingredient. Co-administration with dofetilide, carbamazepine, oxcarbazepine, phenobarbital, phenytoin, rifampicin, rifapentine, proton pump inhibitors, systemic dexamethasone (excluding single dose) or St John's Wort. Warnings/precautions: Risk of hypersensitivity reactions. Discontinue Juluca immediately if suspected. Risks of prolongation of QTc interval, osteonecrosis, opportunistic infections. Monitor LFTs in Hepatitis B/C co-infection and ensure effective Hepatitis B therapy. Small rise in serum creatinine in first 4 weeks of treatment, not considered clinically relevant. Do not co-administer with other antiretrovirals (except in case of co-administration of rifabutin, when an extra dose of rilpivirine 25mg should be used). Use with antacids or once-daily H2-receptor antagonists requires dosage separation. Calcium, iron or multivitamins should be taken at the same time as Juluca with food, otherwise dosage separation recommended. Caution with metformin: monitor renal function and consider metformin dose adjustment to minimise risk of lactic acidosis. If macrolide antibiotics are required, consider azithromycin. Caution with antimalarials (artemether/lumefantrine) or anticoagulants (dabigatran). Pregnancy/ lactation: Not recommended. Avoid breast-feeding. Side effects: See SmPC for full details. Increased total and LDL cholesterol, insomnia, headache, dizziness, nausea, diarrhoea, increased triglycerides, decreased appetite, abnormal dreams, depression, anxiety, sleep disorders, GI disorders, rash, pruritus, fatigue, decreased white blood cell count, haemoglobin and platelet count, arthralgia, myalgia, hypersensitivity, hepatitis, suicidal ideation or suicide attempt, acute hepatic failure. Changes in laboratory biochemistries: elevations of ALT, AST, pancreatic amylase, bilirubin and CPK. Basic NHS costs: £699.02 for 30 tablets (EU/1/18/1282/001). MA holder: ViiV Healthcare UK Ltd, 980 Great West Road, Brentford, Middlesex TW8 9GS. Further information available from Customer Contact Centre, GlaxoSmithKline UK Ltd, Stockley Park West, Uxbridge, Middlesex UB11 1BT.

POM S1A

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Date of approval: May 2018 Zinc code: UK/DTGRPV/0030/18

Adverse events should be reported. For the UK, reporting forms and information can be found at www.mhra.gov.uk/yellowcard or search for **MHRA Yellowcard** in the **Google Play** or **Apple App store**. Adverse events should also be reported to GlaxoSmithKline on 0800 221441.

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Date of preparation: August 2018 UK/DTGRPV/0058/18(1)

More than 40% of the nearly 21 million HIV+ patients being treated today depend on one of our products[1].

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1. 2017 Progress Report on Global Social Responsibility

Date of Publication: August 2018
NON-2018-1207

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More than 40% of the nearly 21 million HIV+ patients being treated today depend on one of our products[1].

Learn more at www.mylan.com

1. 2017 Progress Report on Global Social Responsibility

Date of Publication: August 2018
NON-2018-1207

Mylan
Better Health for a Better World

Descovy® is indicated in combination with other antiretroviral agents for the treatment of adults and adolescents (aged 12 years and older with body weight at least 35 kg) infected with human immunodeficiency virus type-1 (HIV-1).[10]

Odefsey® is indicated for the treatment of adults and adolescents (aged 12 years and older with body weight at least 35 kg) infected with human immunodeficiency virus-1 (HIV-1) without known mutations associated with resistance to the NNRTI class, tenofovir or emtricitabine and with a viral load ≤100,000 HIV-1 RNA copies/mL.[11]

Genvoya® (elvitegravir 150mg/cobicistat 150mg/emtricitabine 200mg/ tenofovir alafenamide 10mg) is indicated for the treatment of human immunodeficiency virus 1 (HIV-1) infection without any known mutations associated with resistance to the integrase inhibitor class, emtricitabine or tenofovir as follows: in adults and adolescents aged from 12 years and with body weight at least 35 kg; in children aged from 6 years and with body weight at least 25 kg for whom alternative regimens are unsuitable due to toxicities.[12]

Prescribing information for Descovy®, Odefsey® and Genvoya® is available overleaf.

All photographs used are not real patients and full permission for their marketing use has been granted.

*Odefsey® is indicated for HIV and is not a treatment for diabetes. However, Odefsey® may be an appropriate choice for HIV patients living with diabetes due to the complexities for this patient group, such as cardiovascular, renal and polypharmacy concerns.

HIV/UK/18-02/MI/1128a(1)a | Date of preparation: June 2018

TRUSTED TRIPLE THERAPY[13,14]

Building on 20 years of a successful treatment approach

DESCOVY® PRESCRIBING INFORMATION

Consult the Summary of Product Characteristics (SPC) before prescribing.

Descovy® ▼ emtricitabine 200mg/tenofovir alafenamide 10mg or 25mg film coated tablets.
Indication: In combination with other antiretroviral agents for the treatment of HIV-1 infection in adults & adolescents (aged 12 years & older weighing at least 35 kg). **Dosage:** Adults & adolescents (aged ≥ 12 years, weighing at least 35 kg): One tablet, once daily, orally with or without food. The dose of Descovy should be administered according to the third agent in the HIV treatment regimen. Please consult the SPC for further information. Children (< 12 years or weighing < 35kg): Safety & efficacy has not been established. Elderly: No dose adjustment is required. Renal: No dose adjustment is required in adult or adolescent patients (aged ≥ 12 years, weighing at least 35 kg) with estimated creatinine clearance (CrCl) ≥ 30 mL/min. In patients with CrCl < 30 mL/min: not recommended. Should be discontinued in patients whose CrCl declines to < 30 mL/min during treatment. Hepatic: no dose adjustment required. **Contraindications:** Hypersensitivity to the active substances or to any excipients. **Warnings & Precautions:** Safety & efficacy in HCV co-infection has not been established. Tenofovir alafenamide is active against HBV. Co-infected HIV/HBV patients should be closely monitored for at least several months following discontinuation for symptoms of severe acute exacerbations of hepatitis. Descovy should be avoided in antiretroviral patients with HIV-1 harbouring the K65R mutation. Risks of mitochondrial dysfunction, immune reactivation syndrome, opportunistic infections, osteonecrosis with CART therapy. **Interactions:** Co-administration with certain anticonvulsants (eg. carbamazepine, oxcarbazepine, phenobarbital & phenytoin), antimycobacterials (eg. rifampicin, rifabutin & rifapentine), boceprevir, St. John's wort and HIV PIs other than atazanavir, lopinavir and darunavir is not recommended. Should not be administered concomitantly with medicines containing tenofovir alafenamide, tenofovir disoproxil, emtricitabine, lamivudine or adefovir dipivoxil. Co-administration of emtricitabine with medicinal products that are eliminated by active tubular secretion may increase concentrations of emtricitabine. Medicinal products that decrease renal function may increase concentrations of emtricitabine. Medicinal products that induce P-glycoprotein (P-gp) are expected to decrease the absorption of tenofovir alafenamide, resulting in decreased plasma concentration of tenofovir alafenamide, which may lead to loss of therapeutic effect of Descovy and development of resistance. Co-administration with medicinal products that inhibit P-gp and breast cancer resistance protein activity is expected to increase the absorption and plasma concentration of tenofovir alafenamide. Tenofovir alafenamide is a substrate of OATP1B1 and OATP1B3 *in vitro*. The distribution of tenofovir alafenamide in the body may be affected by the activity of OATP1B1 and OATP1B3. **Pregnancy & lactation:** Use in pregnancy only if potential benefit justifies the potential risk to the foetus. Breast-feeding; not recommended. **Side effects:** Refer to SPC for full information regarding side effects. Very common (≥1/10): Nausea. Common (≥1/100 to <1/10): Headache, dizziness, diarrhoea, vomiting, abdominal pain, flatulence, abnormal dreams, rash & fatigue. Uncommon (≥1/1000 to <1/100): anaemia, arthralgia, dyspepsia, angioedema & pruritus. **Legal Category:** POM. **Pack:** Bottle of 30 film-coated tablets. **Price:** UK NHS List Price - £355.73; Eire/Ireland – POA. **Marketing Authorisation Number:** EU/1/16/1099/001; EU/1/16/1099/003. Further information is available from Gilead Sciences Ltd, 280 High Holborn, London, WC1V 7EE, UK; Telephone: +44 (0) 8000 113700, For Ireland: +353 214 825 999. E-mail: ukmedinfo@gilead.com. Descovy is a trademark. **Date of approval:** August 2017; DVY/UK/17-08/MM/1194

GENVOYA® PRESCRIBING INFORMATION

Consult the Summary of Product Characteristics (SPC) before prescribing.

GENVOYA® ▼ elvitegravir 150mg/cobicistat 150mg/emtricitabine 200mg/tenofovir alafenamide 10mg film coated tablets.
Indication: Treatment of HIV-1 infection without known mutations associated with resistance to the integrase inhibitor class, emtricitabine or tenofovir in adults & adolescents (aged 12 years & older weighing ≥ 35 kg and children aged from 6 years and with body weight ≥ 25 kg for whom alternative regimens are unsuitable due to toxicities. **Dosage:** Adults & paediatric patients aged 6 years or older, weighing ≥ 25 kg: One tablet, once daily, orally & whole with food Children (< 6 years or weighing < 25kg): Safety & efficacy has not been established. Elderly: No dose adjustment required. Renal: No data are available to make dose recommendations in children aged less than 12 years with renal impairment. No dose adjustment is required in adult or adolescent patients (aged ≥ 12 years, weighing at least 35 kg) with estimated creatinine clearance (CrCl) ≥ 30 mL/min. In patients with CrCl < 30 mL/min: not recommended. Should be discontinued in patients whose CrCl declines to < 30 mL/min during treatment. Hepatic: Mild/moderate hepatic impairment: no dose adjustment required. Severe hepatic impairment: not recommended. **Contraindications:** Hypersensitivity to the active substances or to any excipients. Coadministration with medicinal products that are highly dependent on CYP3A for clearance and for which elevated plasma concentrations are associated with serious or life threatening adverse reactions, and CYP3A inducers. **Warnings & Precautions:** Should not be co-administered with other antiretroviral products. Safety & efficacy in HCV co-infection has not been established. Tenofovir alafenamide is active against HBV. Co-infected HIV/HBV patients should be closely monitored for at least several months following discontinuation for symptoms of severe acute exacerbations of hepatitis. Should not be administered concomitantly with medicines containing tenofovir alafenamide, tenofovir disoproxil, lamivudine or adefovir dipivoxil for treatment of HBV infection. Patients with galactose intolerance, Lapp lactase deficiency & glucose-galactose malabsorption should not take Genvoya. Women of childbearing potential should use either a hormonal contraceptive containing at least 30 µg ethinylestradiol & containing drospirenone or norgestimate as the progestagen or an alternative reliable method of contraception. Risks of mitochondrial dysfunction, immune reactivation syndrome, opportunistic infections, osteonecrosis with nucleoside analogues & CART therapy. **Pregnancy & lactation:** not recommended. Should not be used whilst breast-feeding. **Side effects:** Refer to SPC for full information regarding side effects. Very common (≥1/10): Nausea. Common (≥1/100 to <1/10): Headache, dizziness, diarrhoea, vomiting, abdominal pain, flatulence, abnormal dreams, rash & fatigue. **Legal Category:** POM. **Pack:** Bottle of 30 film-coated tablets. **Price:** UK NHS List Price - £879.51; Eire/Ireland - POA. **Marketing Authorisation Number:** EU/1/15/1061/001 Further information is available from Gilead Sciences Ltd, 280 High Holborn, London, WC1V 7EE, UK; Telephone: +44 (0) 8000 113700. E-mail: ukmedinfo@gilead.com. Genvoya is a trademark. **Date of approval:** March 2018. Job Bag No: GNV/UK/18-03/MM/1094

ODEFSEY® PRESCRIBING INFORMATION

Consult the Summary of Product Characteristics (SPC) before prescribing.

Odefsey® ▼ emtricitabine 200mg/ rilpivirine 25mg/ tenofovir alafenamide 25mg film coated tablets.
Indication: Treatment of HIV-1 infection in adults & adolescents (aged 12 years & older weighing at least 35 kg) without any known mutations associated with resistance to the non-nucleoside reverse transcriptase inhibitor class, tenofovir or emtricitabine and with a viral load ≤ 100,000 HIV-1 RNA copies/mL. **Dosage:** Adults & adolescents (aged ≥ 12 years, weighing at least 35 kg): One tablet, once daily, orally with food. Children (< 12 years or weighing < 35kg): Safety & efficacy has not been established. Elderly: No dose adjustment is required. Renal: No dose adjustment is required in adult or adolescent patients (aged ≥ 12 years, weighing at least 35 kg) with estimated creatinine clearance (CrCl) ≥ 30 mL/min. In patients with CrCl < 30 mL/min: not recommended. Should be discontinued in patients whose CrCl declines to < 30 mL/min during treatment. Hepatic: Mild/moderate hepatic impairment: no dose adjustment required. Use with caution in patients with moderate hepatic impairment. Severe hepatic impairment: not recommended. **Contraindications:** Hypersensitivity to the active substances or to any excipients. It should not be co administered with medicines that can result in significant decreases in rilpivirine plasma concentrations (due to cytochrome P450 [CYP]3A enzyme induction or gastric pH increase), which may result in loss of therapeutic effect of Odefsey including: carbamazepine, oxcarbazepine, phenobarbital, phenytoin, rifabutin, rifampicin, rifapentine, omeprazole, esomeprazole, dexlansoprazole, lansoprazole, pantoprazole, rabeprazole, dexamethasone (oral and parenteral doses), except as a single dose treatment, St. John's wort. **Warnings & Precautions:** There are insufficient data to justify the use in patients with prior NNRTI failure. Resistance testing and/or historical resistance data should guide the use of Odefsey. At supratherapeutic doses (75 mg once daily and 300 mg once daily), rilpivirine has been associated with prolongation of the QTc interval of the electrocardiogram (ECG). Should be used with caution when co administered with medicines with a known risk of Torsade de Pointes. Safety & efficacy in HCV co-infection have not been established. Tenofovir alafenamide is active against HBV. Co-infected HIV/HBV patients should be closely monitored with both clinical and laboratory follow up for at least several months following discontinuation for symptoms of severe acute exacerbations of hepatitis. The safety and efficacy of Odefsey in patients with significant underlying liver disorders have not been established. Risks of mitochondrial dysfunction, immune reactivation syndrome, opportunistic infections, osteonecrosis with CART therapy. Should not be co-administered with other antiretroviral medicines or with other medicines containing tenofovir alafenamide, lamivudine, tenofovir disoproxil or adefovir dipivoxil. **Interactions:** Co-administration of emtricitabine with medicines that are eliminated by active tubular secretion may increase concentrations of emtricitabine and/or the co administered medicines. Medicines that decrease renal function may increase concentrations of emtricitabine. Rilpivirine is primarily metabolised by CYP3A. Medicines that induce or inhibit CYP3A may thus affect the clearance of rilpivirine. Medicines that induce P-glycoprotein (P-gp) are expected to decrease the absorption of tenofovir alafenamide, resulting in decreased plasma concentration of tenofovir alafenamide, which may lead to loss of therapeutic effect of Odefsey and development of resistance. Co-administration with medicines that inhibit P-gp and breast cancer resistance protein activity is expected to increase the absorption and plasma concentration of tenofovir alafenamide. Tenofovir alafenamide is a substrate of OATP1B1 and OATP1B3 *in vitro*. The distribution of tenofovir alafenamide in the body may be affected by the activity of OATP1B1 and OATP1B3. **Pregnancy & lactation:** Avoid use in pregnancy. Lower exposures of rilpivirine (one of the components of Odefsey) were observed during pregnancy; therefore viral load should be monitored closely. Alternatively, switching to another antiretroviral regimen could be considered. Breast-feeding; not recommended. **Side effects:** Refer to SPC for full information regarding side effects. Very common (≥1/10): increased total cholesterol (fasted), increased LDL cholesterol (fasted), insomnia, headache, dizziness, nausea, increased pancreatic amylase, increased transaminases (AST and/or ALT). Common (≥1/100 to <1/10): decreased white blood cell count, decreased haemoglobin, decreased platelet count, decreased appetite, increased triglycerides (fasted), depression, abnormal dreams, sleep disorders, depressed mood, somnolence, abdominal pain, vomiting, increased lipase, abdominal discomfort, dry mouth, flatulence, diarrhoea, increased bilirubin, rash, fatigue. Uncommon (≥1/1000 to <1/100): anaemia, immune reactivation syndrome, dyspepsia, severe skin reactions with systemic symptoms, angioedema, pruritus, arthralgia. **Legal Category:** POM. **Pack:** Bottle of 30 film-coated tablets. **Price:** UK NHS List Price - £525.95; Eire/Ireland – POA. **Marketing Authorisation Number:** EU/1/16/1112/001; EU/1/16/1112/002. Further information is available from Gilead Sciences Ltd, 280 High Holborn, London, WC1V 7EE, UK; Telephone: +44 (0) 8000 113700, For Ireland: +353 214 825 999. E-mail: ukmedinfo@gilead.com. Odefsey is a trademark. **Date of approval:** January 2018; ODE/UK/18-01/MM/1001

▼ This medicinal product is currently subject to additional monitoring. Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Any suspected adverse reactions to Descovy, Genvoya or Odefsey should be reported to Gilead via email to Safety_FC@gilead.com or by telephone +44 (0) 1223 897500.

Adverse events should be reported. For the UK, reporting forms and information can be found at www.yellowcard.mhra.gov.uk

For Ireland, suspected adverse reactions should be reported to the HPRA Pharmacovigilance using a Yellow Card obtained either from the HPRA, or electronically via the website at www.hpra.ie. Adverse reactions can also be reported to the HPRA by calling +353 1 6764971.

REFERENCES:
1. Sax P, *et al*. Lancet 2015; 385: 2606–2615. **2.** Eron J, *et al*. EACS 2017. Abstract PS8/2. **3.** Gaur A, *et al*. Lancet HIV 2016; 3: e561–568. **4.** Mills A, *et al*. Lancet Infect Dis 2016; 16(1): 43–52. **5.** Winston A *et al*. EACS 2017. **6.** Orkin C, *et al*. Lancet HIV 2017; http://dx.doi.org/10.1016/S2352-3018(17)30179-0 [Accessed February 2018]. **7.** Gilead Sciences. Data on File HIV-UK-17-03. **8.** Wohl D, *et al*. J Acquir Immune Defic Syndr 2016; 72: 58–64. **9.** Arribas J, *et al*. J Acquir Immune Defic Syndr 2017; 75: 211–218. **10.** SmPC Descovy®. Available at: https://www.medicines.org. uk/emc/medicine/31764 and https://www.medicines.org. uk/emc/history/31765. Accessed February 2018. **11.** SmPC Odefsey®. Available at http//www.medicines.org.uk/emc. **12.** SmPC Genvoya®. Available at http//www.medicines.org.uk/emc. **13.** European AIDS Clinical Society (EACS) guidelines. Version 8.2, January 2017. Available at: http://www.eacsociety.org/files/guidelines_8.2_english.pdf. Accessed February 2018. **14.** US Department of Health and Human Services (DHHS). July 2016. Guidelines for the use of antiretroviral agents in HIV-1-infected adults and adolescents. Available at: http://aidsinfo.nih.govguidelines. Accessed February 2018.

ABBREVIATIONS:
CrCl, Creatinine Clearance.
NNRTI, non-nucleoside reverse transcriptase inhibitor

GILEAD