Service Improvement

Does the HIV speciality have a streamlined education and training programme for pre-registration pharmacists at your institution?

My passion for working within HIV started during my pre-registration year at Queen Elizabeth Hospital Birmingham (QEHB) teaching hospital. Part of my training included a rotation in the outpatient HIV clinics. Sitting in with various healthcare professionals (HCPs) who were so passionate about their speciality really left a positive impression on me. Three years later I am now working as a Specialist Pharmacist at QEHB alongside those who trained me!

Having always had an interest in education and training it was only natural for me to want to create a robust training structure to motivate, inspire and encourage other students. Looking back at my own experiences, it was those lecturers and teachers that were inspirational and passionate about their speciality that stuck in my mind.

It has always been important for me to pass on my knowledge to my colleagues, be that inter- or intra-professionally. Of course in the busy role of a pharmacist, creating a structured education and training programme per speciality is sometimes a vision of the future. We are often on a continuous cycle of transferring this from one to-do list to the next! However, the importance of bringing training to the forefront of our pharmacy careers has never been clearer.

When speaking to a number of students it was apparent that there are differences in the way in which HIV is taught at University, if at all. It is our role as specialist pharmacists to ensure that we bridge and consolidate this learning. To tackle this I created an in house pre-registration pharmacy manual specific for the HIV speciality. The aims for implementing this were to:

1. Create a structured and standardised manual for all pre-registration pharmacists who spend time in the HIV clinics at QEHB.

2. Teach students about the basics of HIV including procedural, clinical and and ethical practices.

3. Inform students about the commonly used resources for the HIV speciality so that reviewing these patients is less daunting!

4. Introduce students to as many HCPs as possible so that they feel more comfortable speaking to them during their pharmacy careers.

5. Develop a positive learning environment encouraging students to take ownership of the opportunities to learn and develop.

The pre-registration pharmacy manual consisted of key teaching areas including procedural, clinical and ethical practices when working at the HIV clinic at QEHB. Key aspects were as follows:

1. **Procedural**: introduction to clinic area/ layout and processes, clinic services and pharmacy services.

2. **Clinical**: HIV transmission, anti-retroviral choices and rationale, adherence, interactions, resistance, travel including anti-malarial medication, Post-exposure Prophylaxis (PEP) and Pre-exposure Prophylaxis (PrEP), pregnancy and clinical trials. This also includes shadowing at least three HCPs in addition to pharmacists such as doctors, nurses, health advisors, dieticians and social workers.

3. **Ethical**: awareness of stigma, confidentiality, issues around disclosure and presenting real life scenarios.

Building on the foundations of the students existing knowledge correlates well with the General Pharmaceutical (GPhC) Pharmacist pre-registration manual which uses Miller's Triangle of competence to ensure a progressive curriculum (1).

In addition to these key aspects, professionalism is a key feature of the GPhC pharmacy standards (2) and the Trusts values. Pre-registration pharmacists will intentionally and unintentionally pick up on the actions and behaviours of those around them and so it is vital that we as HCPs lead by example.

There is always room for improvement for all services and so we have always encouraged students

Service Improvement

that spend time with us to provide us with constructive feedback. The manual has a form included whereby students can evaluate their experience during the HIV rotation. Here are some examples of the comments that the HIV team has received:

After roll out of this initiative I also had very positive feedback from our senior pharmacy managers and education and training leads. This has led to the manual being adapted for fourth year pharmacy students, medical students and other HCPs throughout the Trust. Aspects of the manual have also been integrated into the Trust pharmacist induction programme. I am sure that as the manual is utilised more and more there will be further changes and re-evaluations.

Overall, it has been a positive, valuable and insightful experience. Bringing education and training to the forefront and regularly evaluating our teaching methods will ensure the best possible learning environment. This in turn will lead to confident and competent pharmacists. As Marian Wright Edelman said "Education is for improving the lives of others and for leaving your community and world better than you found it."

With special thanks to the HIV pharmacists and the multi-disciplinary team at QEHB who take the time to inspire and teach our students.

Miss Hammara Sattar
Queen Elizabeth Hospital (Part of University Hospitals Birmingham)

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Service Improvement

A Malaria Prevention Service provided through a community pharmacy multiple

As Independent Pharmacist Prescribers prescribing for a community pharmacy malaria prevention service we see a range of travellers and frequently encounter complex travellers, i.e. those with complex itineraries and/ or complex medical conditions. With improved convenience and accessibility to services through community pharmacy, located where people live and work, we regularly see people living with HIV requesting antimalarials. Travel health professionals in England and Wales follow Public Health England's Guidelines for Malaria Prevention in travellers from the UK. Specific advice is included for people living with HIV and travel health professionals are advised to liaise with the traveller's HIV physician on choice of antimalarials.

A thorough risk assessment takes place in the pharmacy and details of all medicines and medical conditions are recorded. The patient is asked to provide details of their HIV clinic and they are made aware that we will contact their HIV team and give their consent. The consultation details escalate to a prescribing pharmacist for consideration. Using the Liverpool HIV interaction checker possible options and considerations for the traveller based on the drug-drug interaction information are determined. Other reference sources are also used to establish any other factors which could influence the decision of which antimalarial is preferable for the traveller. For example, the Summary of Product Characteristics for Lariam (mefloquine) states that concomitant administration of mefloquine with other drugs known to alter cardiac conduction (e.g. anti-arrhythmic or beta-adrenergic blocking agents, calcium channel blockers, antihistamines or tricyclic antidepressants) might also contribute to a prolongation of the QTc interval.
The prescribing pharmacist makes the decision about suitable antimalarials and contacts the HIV clinic to check that the reported medicines are correct and to discuss their recommendation for antimalarials. The team has the opportunity to provide any additional information they feel is relevant.

Additionally for those who are visiting countries with a low risk of malaria we check with the HIV team whether the person is immunocompromised, because anyone who is immunocompromised should consider antimalarials even for low risk areas where other travellers would not normally require antimalarials.

All travellers are provided with written information to help them stay healthy during their trip and they are also give traveller-specific information leaflets. Our leaflet for people living with HIV includes information about country entry requirements, travelling with medication, and a list of useful websites.

<u>Using opportunities for advice about pre-travel health</u>
One of the key factors in educating travellers about malaria prevention is in ensuring the messages reach them about the importance of seeking advice and the value in taking antimalarials when indicated. Those travellers who are visiting friends and relatives (VFRs) are a hard-to reach group where it is known that VFR travellers have a higher tendency to travel at the last minute and many have different attitudes to the potential health risks of travel. In 2018, 85% of malaria cases imported into the UK (where the reason was known) were among people who were VFRs.

Making every contact count (MECC) is an approach to behavioural change, supported by Public Health England, that utilises the millions of day to day interactions that organisations and people have with other people to encourage changes in behaviour that have a positive effect on the health and wellbeing of individuals, communities and populations. The changes highlighted under this initiative such as stopping smoking, improving diet, increasing physical activity, losing weight and reducing alcohol consumption can help people to reduce their risk of poor health significantly. Given the serious consequences of malaria, and the possibility that these may be even more serious for those travellers who are immunocompromised, we would propose that the principles of MECC are equally applicable to the specialist area of pre-travel advice for those diagnosed with HIV.

For community pharmacists supplying medicines to people living with HIV, messages about seeking pre-travel advice if the person

intends to travel in the future can be provided when counselling patients. Although the NHS recommends that where possible, people seek travel advice at least 8 weeks before departure, many people travel last minute for a variety of reasons and it is recognised that this timeframe is not always possible. Reasons include travelling for business, family emergencies overseas, visiting friends and relatives, the growing popularity and availability of holidays booked online. In such cases, people are not always able to plan their travel health in advance.

Pharmacy teams in both primary and secondary care have an opportunity to reinforce the importance of seeking pre-travel advice in good time. Last minute travel plans however, should be no barrier to a person seeking advice and every contact with a person living with HIV can be used to educate them on the health benefits of pre-travel health advice and raise awareness of the options available to access this advice. With extended opening hours, including late nights and weekends and even availability of travel clinics in pharmacies located at airports, accessibility to travel health advice has improved for all travellers, including those travelling last-minute.

Opportunities exist in primary and secondary care to educate those who may consider travel at some point in the future. By using each opportunity to reinforce messages about measures to protect their health, pharmacists have a vital role to play in helping travellers living with HIV to take positive action to protect themselves against malaria.

Jan Jones and Patricia Armstrong
Boots Specialist Practitioner
Independent Prescribers

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Service Improvement

The impact of the introduction of a specialist HIV pharmacy service (SHPS) to satellite HIV clinics

In January 2018, I started a job as a Highly Specialist HIV Pharmacist under Chelsea and Westminster NHS Foundation Trust (CWFT), with the primary role of implementing and establishing a specialist HIV pharmacy service to 3 satellite HIV outpatient clinics based in/around Hertfordshire (Stevenage, Watford and Harlow). The 3 sites consisted of approximately 1050 patients in total.

I'd like to share my experience from my involvement in implementing this service; achievements and challenges in the role, and my experience on presenting this project as an oral presentation at the BHIVA Spring 2019 conference.

In 2015, CWFT acquired the 3 satellite HIV outpatient clinics. These clinics and their HIV MDTs had no HIV pharmacist input. Antiretroviral (ARV) prescriptions were remotely screened by a non-specialist pharmacist, with no access to patient notes or blood results, and no pharmacy support was directly available for patients or staff. ARV prescriptions were, and are still, dispensed either at the local hospital, with which we have an SLA, or via home delivery.

In 2017 a 1day/week HIV pharmacy service was introduced to the Stevenage clinic. The Lead pharmacist and Lead clinicians, worked closely with stakeholders and the CWFT contracts team to secure funding for a 2.5 days/week specialist pharmacist on a 1 year fixed-term contract, which is the role I commenced in January 2018. My role included collecting data on the impact of the implementation of the service, which would be used to support a business case for a permanent specialist HIV pharmacist in the clinics.

As fellow HIV pharmacists and technicians, we know the value of our speciality within the HIV MDT and our significant contributions to patient safety, cost-efficiencies and drug savings, and patient experience, so I am sure you would share my concerns at the thought of an HIV clinic without any specialist pharmacy support (!).

The aims of specialist HIV pharmacy service were based around national, regional and local guidance and standards of care, as per Figure 1 on the poster below. The primary roles of the HIV pharmacist in the clinic involved screening antiretroviral prescriptions, participating in the weekly MDTs, providing pharmaceutical advice to healthcare professionals and patients, and setting up a pharmacist-led treatment support clinic in which patients were booked in to discuss starting/switching ARVs or medication queries.

The impact of the implementation of the service was measured through 4 methods; (1) Prospective recording of pharmacy-led interventions; (2) Drug-savings data through CQUINS and QIPPs; (3) Review of the pharmacist-led treatment support clinics; (4) Staff service evaluation survey. These, and the results, are discussed in detail in the poster below.

It was clear that the implementation of a specialist HIV pharmacy service in the clinics led to improvements in patient safety, drug-savings and efficient use of the MDT staff skill-mix, and provided pharmaceutical support to patients and the HIV MDT. Implementation of the service also meant that the clinics were now meeting local, regional and national guidance and standards or care for HIV outpatient clinics, which were previously unmet. From this data collection, the specialist HIV pharmacist contract was extended for a further 12months, and we are now working on securing a permanent full-time contract.

There were some limitations to the data collection, as there was only one part-time pharmacist in the role and collecting the data, time-constraints meant that some interventions may not have been recorded and therefore this is an underestimation of pharmacist-led interventions which were made. Collecting patient feedback would have been valuable data, but was unfortunately not feasible in the time.

There were challenges in implementing the service. All 3 clinics were well established prior to the introduction of the pharmacy service, which meant processes related to prescriptions were already in place. In a busy clinic, in which clinicians are already pushed

for time, changing processes added additional stress. It was important for me to understand the current processes and communicate with, and involve key staff members, when suggesting change and implementing new processes, and to gain constructive feedback on what worked well and what didn't. The role itself also has its difficulties, as it is a part-time role spread across 3 different geographical locations, all with different IT, paper notes and EPR systems, which makes continuity of the service challenging. In addition to this, as the contract is currently fixed-term, this can cause difficulties in planning ahead for the service. Securing a permanent, full-time contract will help to overcome these challenges and allow the service to be developed further, for example, setting up non-medical prescribing clinics.

With the support of my co-authors (all of whom, prior to my involvement, were instrumental in setting up the service), I submitted this project as an abstract for the BHIVA Spring 2019 conference. The abstract was selected to be presented as an oral presentation at the conference - I was surprised, excited and nervous! I didn't expect a pharmacy practice focused project to be selected for an oral presentation, but in fact it just reflected the value of the specialist pharmacist within the HIV MDT. I hadn't been to a BHIVA conference before, so I was not sure what to expect. I'm not a keen public speaker, so I practiced my presentation at every opportunity; in front of clinicians, MDTs and my family and friends, and gained constructive feedback from my co-authors, all of which improved my confidence in public speaking and helped me to prepare for questions I may be asked. It was a great experience presenting at a national conference, the audience appeared engaged and asked relevant questions, and I received some positive and encouraging feedback. It reminded me how important it is for us to share our pharmacy practice research, and I would encourage other pharmacists and technicians to share their research from service development projects.

Naman Vora

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The impact of the introduction of a specialist HIV pharmacy service (SHPS) to satellite HIV clinics

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[1]Chelsea and Westminster Hospital NHS Foundation Trust (CWFT); [2]Kingston Hospital NHS Foundation Trust (CWFT at time of data collection); [3]Gilead Sciences, Ltd (CWFT at time of project).

Disclosure: Gilead Sciences have not had any involvement with this project.

Background

BHIVA Standards of Care[1] recommend specialist HIV pharmacy provision within HIV services. In 2015, our NHS Hospital Foundation Trust acquired 3 satellite HIV outpatient clinics based in Hertfordshire; Clinics A, B and C, consisting of approximately 1050 patients in total.

At the time, the clinics and HIV multi-disciplinary team (MDT) had no HIV pharmacist input. Antiretroviral (ARV) prescriptions were screened remotely by a non-specialist pharmacist, with no access to patient notes/bloods and no pharmacy support was directly available for patients or staff.

In April 2017, a specialist HIV pharmacy service (SHPS) was implemented in Clinic A, and in January 2018 expanded to include Clinics B and C. The aims of the SHPS were based on local and national standards of care and guidance, as illustrated in figure 1.

A 0.5WTE specialist HIV pharmacist now covers the 3 clinics, on a fixed-term post. A service evaluation was undertaken to assess the impact of the SHPS.

Standards and guidance
• Hackett Report, Department of Health and Royal Pharmaceutical Society[2]
• BHIVA Standards of Care[1]
• NHSE Clinical Reference Group Service Specifications[3]
• NHSE Clinical Reference Group MDT Standards[3]
• NHSE Regional ARV guidance[4]
• Lord Carter Report[5]
• NICE Medicines Optimisation[6]

Aims of SHPS
• clinically screen ARV prescriptions
• improve patient safety
• counsel patients on ARVs
• support the MDT
• support cost-effective use of ARVs
• support prescribing to guidelines
• reduce medication wastage
• reduce time spent by non-pharmacy staff dealing with medication queries

Figure 1. Aims of the specialist HIV pharmacy service (SHPS), and national and local guidance/standards the SHPS aims to comply with

Methods

A service evaluation was undertaken to assess the impact of the SHPS, via 4 methods:

1. **Pharmacy-led interventions** were prospectively recorded over a 15month period at Clinic A and a 10month period at Clinics B and C. Interventions were categorised into 8 different categories; drug-drug interactions (DDIs), other clinical interventions (e.g. identifying potential ARV switches or rationalising ARV regimes), patient counselling, patient safety (e.g. responding to MHRA Drug Safety alerts, i.e. dolutegravir use in pregnancy alert), reduction of drug wastage, proactive patient follow-up and engagement (patients identified as overdue clinic review or requiring early follow-up), medication errors and prescription quantity adjustment
2. **Drug savings data** was prospectively recorded over a 12month period at Clinic A. This was through CQUINs/QIPPs from Atripla to Truvada/generic Efavirenz (TFV/gEFV) and Kivexa to generic Abacavir/Lamivudine (gABC/3TC) switches
3. The **pharmacist-led treatment support clinic** at Clinic A was retrospectively reviewed over a 10month period
4. A **service evaluation survey** was sent to 16 HIV MDT members across all 3 sites

Results

Results 1: Pharmacist-led interventions

- 789 interventions were made over a 15month period across 3 sites, as per figure 2.
- The majority of interventions were related to prescription quantity adjustments, patient follow-up and engagement, and other clinical interventions
- 6% of the interventions were DDIs, which were re-categorised using the Liverpool HIV Drug Interactions website[7] traffic light system in the bar chart, as per Figure 2
- 20% of the DDIs identified were red contraindications. 29% of the DDIs identified were marked as 'other' for drugs not currently on the Liverpool website, and for which severity couldn't be ranked i.e. certain herbal supplements

Results 2: Savings through QIPPs/CQUINs

- A total of ~£98,000 was saved through pharmacist-led generic switches alone, at Clinic A over a 12month period
- The majority of switches were pharmacist-led. 97% of Kivexa to gABC/3TC, and 67% of Atripla to TRV/gEFV switches were pharmacist-led
- By making these drug-savings, we fully achieved our CQUIN

Results 3: MDT survey feedback

- 13/16 MDT members completed the anonymous staff survey
- 100% of MDT members felt the SHPS improved patient safety
- 100% of MDT members felt the SHPS was a valuable member of the MDT

Example comment from MDT feedback, regarding impact of SHPS:
'Hugely increased patient safety, excellent source of invaluable information and enables a better service for patients and better working for clinicians'

Results 4: Pharmacist-led Clinic

- 124 appointments were made in the pharmacist-led clinic at Clinic A over a 10month period, for consultations as categorised in table 1
- The pharmacist-led clinics support efficient use of the HIV MDT staff-skill mix, as prior to the SHPS, these appointments would have been booked with a consultant or CNS

Type of appointment	Number of appointments
Starting/switching ARVs	89
DDI	11
Side-effects advice	8
Adherence support	7
Other	9
Total	**124**

Table 1. Review of the pharmacist-led clinic

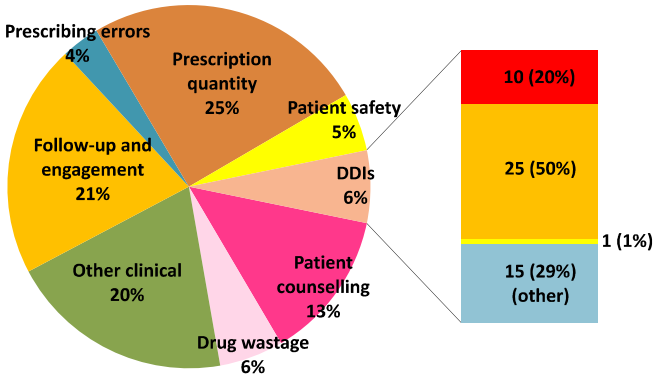

Figure 2. Pharmacist-led interventions recorded over a 15month period (n = 789)

Key challenges in implementing service

- The SHPS is currently a part-time role (2.5days/week), with no cover for sickness and leave, making continuity of the service challenging
- The role requires cross-site working at 3 geographically separate locations
- The IT, EPR and (paper) notes systems differ at each site, making cross-site working difficult
- The post is currently on a fixed-term contract, resulting in uncertainties for future service development

Conclusions

Implementation of the SHPS has led to, and supported:

- ✓ Improvements in patient safety
- ✓ Cost-saving delivered on ARVs
- ✓ Specialist HIV pharmacist advice to patients and HCP
- ✓ Meeting national, regional and Trust standards of care and guidance
- ✓ Improved use of staff skill-mix

Based on data from this service evaluation, funding for the SHPS has been extended for a further 12months and we are formulating a business case for a permanent SHPS post in the satellite clinics. There are opportunities for further service development e.g. non-medical prescribing clinics.

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Service Improvement

HIV Multi-Disciplinary Team for patients aged 50 or over

Background
Meeting the needs of the older patient living with HIV is particularly pertinent at County Durham and Darlington NHS Foundation Trust (CDDFT), where 50% of our cohort will be aged 50 or over within the next 5 years.
The multi-disciplinary team (MDT) consists of a primary care practitioner, HIV clinicians, a specialist HIV pharmacist and nurse practitioner.
The MDT aims to address some of the complex needs and unique challenges of the older patient living with HIV, including:

- HIV being an additional risk factor for chronic disease, such as cardiovascular disease, diabetes and metabolic disorders
- HIV medication exacerbating cardiovascular, renal and bone disorders
- Patient preference regarding disclosure can limit communication between primary and secondary care (50% of our cohort do not permit us to correspond with their GP)

Method
A monthly programme of virtual review at MDT is scheduled, using web-cam technology. MDT members are able to take part across three hospital sites at the Trust.
An MDT pro forma has been designed to record monitoring and screening, in line with BHIVA monitoring guidelines (www.bhiva.org). Drug interactions are checked, and recommendations are made on anti-retroviral regimen (ARV) optimisation.
MDT recommendations are recorded in patient notes and are communicated to the patient's GP, where consent allows.
'A patient self-management plan' is agreed at MDT, to be communicated at the next HIV clinic appointment. In this way it is hoped that increased self efficacy will encourage patients to address lifestyle factors, access services and engage in conversation regarding disclosure to their GP.

Results
The project is just getting started, and a few patients so far have been reviewed in this MDT process.
Outcome measures will assess:

- The proportion of > 50yrs HIV population reviewed by MDT
- The proportion of patients meeting minimum standards of monitoring and screening (pre/post MDT)
- Where medication review at MDT resulted in a change in ARV regimen
- Where new drug interactions were identified at MDT
- Where MDT review resulted in recognition of additional health needs
- The proportion of previously non-consenting patients who allow HIV consultants to communicate with their GP following discussion of MDT recommendations
- The proportion of primary care physicians who receive written communication of MDT recommendations (in those who are consented)

Impact assessment will be completed at the end of the project to inform it's utility and if successful, additional funding via business case sought to secure sustainability of the project in the longer term.

Please note this project was sponsored by Gilead, who awarded a fellowship grant.

Dr S Duncan, Ms Jill Ross, Dr S Ralph, Dr C White, Dr A Wardropper
CDDFT Sexual Health Services

Conference Feedback

STI & HIV 2019 World Congress

The Joint Meeting of the 23rd ISSTDR and 20th IUSTI was held in Vancouver Canada between 14 –17 July 2019 under the theme of 'The Evolving Landscape of STI and HIV Elimination.' My attendance at this biennial meeting offered me the opportunity to hear the latest scientific developments from world leaders in the STI/HIV field.

The opening keynote lecture delivered by Rino Rappuoli drew our attention to the achievable possibility of the development of bacterial STI vaccines. Mr Rappuoli has been extensively involved in the development of GSK meningitis vaccines ACWY and more recently the meningitis B vaccine Bexsero. The vaccine was developed using a technique known as "reverse vaccinology" which identified novel antigens and epitopes from the genomic profile of the bacteria, which may be potential vaccine targets.
Bacterial meningitis is caused by Neisseria meningitides and the development of meningitis B vaccine has been shown to induce antibodies that target Neisseria gonorrhoea. These findings pave the way for further research to develop a gonorrhea specific vaccine, and they provide evidence to justify human trials to confirm Bexsero-induced protection against gonorrhea.

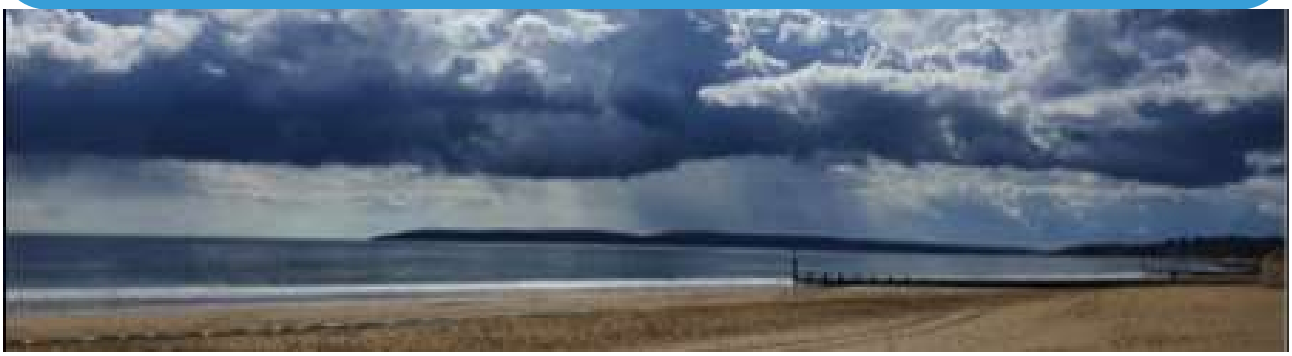
There were thought provoking global health lectures highlighting the progress which has been made towards the UNAIDS 90-90-90 target in the era of combination prevention and celebrating the success of many combination prevention approaches including TasP, voluntary male medical circumcision and PrEP. But also sobering discussions from a representative from the World Bank - David Wilson with regards to the global HIV response, and whether we should expect more from the $13billion of developmental aid which has funded access to cART for 23million PLWHIV worldwide. He also addressed the challenges facing middle-income countries to adopt the strategies successful in advancing HIV treatment over the last 40years to improve wider population health outcomes with regards to childhood immunisations and prevention of non-communicable diseases.

Challenges on improving the equity and effectiveness of sexual health care brought gender identity to the fore, with results from the 2017 EMIS (European MSM Internet Survery) highlighting the barriers to accessing appropriate sexual health tests due to the stigma facing MSM in eastern European countries disclosing sexual orientation. This was brought closer to home by Lorraine McDonagh (University College London) who briefly mentioned the reduction in funding to specialised sexual health services in the NHS which has shifted asymptomatic STI screening into GP practices. Lorraine presented qualitative research into accessibility of these services by the young LGBTQ community and the prejudices faced within urban and rural settings. This made me reflect on the provision of sexual health care locally and how we as healthcare providers need to build networks with primary care providers to help support and educate our colleagues in navigating the evolving nature of gender fluidity.
An article in the Lancet 2016 reported that there were 25 million transpeople worldwide and as healthcare providers we need to be asking the appropriate questions to best identify these populations when capturing demographic information. Questions such as "What is your current gender?" and "What sex were you assigned at birth?" help to open these lines of communication and dialogue.

This was an internationally renowned conference which hailed global experts and afforded me the opportunity to reflect on our local practice and adopt measure to improve patient outcomes.

Bronagh McBrien
Manchester Foundation Trust

Conference Feedback



BHIVA Spring Conference 2019 Highlights

The 25th annual BHIVA conference was held in Bournemouth in April with 486 delegates making the trip to the coast. This was my first time at BHIVA and I was in awe of the wealth of talks and the plethora of interesting posters in the exhibition hall. Here are a few of my highlights…

The conference pre-meeting was centred on U=U. The language we use when discussing this with people living with HIV (PLWH) is so important. Evasive language such as "negligible", "extremely low", "virtually impossible" will undermine the patient's confidence in U=U. PARTNER and PARTNER2 are ground-breaking studies that demonstrate ZERO or NO risk of transmission when someone's viral load is undetectable and that is the direct language we must be using. U=U founder Bruce Richman did an inspiring talk about the effect U=U has had on the HIV community, how this message is so important to tackle HIV stigma and how transformative it has been for people to have sex without the fear of transmission. He has done some incredible work to get this message out there but there is still such a lot of work to be done especially in lower income countries. We can all contribute and make sure every person we see knows about U=U!

The much anticipated data for the injectable cabotegravir/rilpivirine was presented by Prof Chloe Orkin. Virological suppression and virological non-response rates were similar in the injectable versus oral treatment groups. Injection site reactions were predictably high but these were mostly mild-moderate, resolved within 7 days and became less frequent as the study continued. Interestingly and which surprised me, in a single question preference survey at week 48, a massive 99% of the participants preferred the injections to oral therapy!

Another anticipated presentation came from Laura Waters on "The London patient", a sequel, so to speak, to "The Berlin patient". Both patients received stem cell transplants from a Δ 32 donor. A Δ 32 mutation is rare, only 1% of Europeans are Δ 32 homozygous and resistant to R5 HIV-1. Following the transplant the patient had loss of CCR5 expression on CD4/8 cells and remains undetectable using ultra-sensitive assays off ARVs after more than 2 years. Another step forward in the search for a cure.

The POPPY sleep study was an intriguing presentation. It compared the quality of sleep in PLWH compared to HIV negative controls. Quality of sleep was measured by wearing a device that captured actigraphy data. Self-reported insomnia was much higher in PLWH (22.6%) compared to the HIV negative group (6%) but actual sleep duration and efficiency was the same between the groups and the majority of the PLWH showed sleep duration and efficiency above standards thresholds of poor sleep quality.

MSD put on a unique symposium in the style of "Dragon's Den". They, of course, had a "dragon" pitching their latest NNRTI, Doravirine, which was met with some trepidation with a general feeling that it is alitte late to the game in the era of integrase inhibitors. However, no food requirements, few interactions, once daily dosing, added flexibility of having an individual tablet, fewer CNS side effects, favourable lipid profile and little resistance in the trials ultimately lead to 2 out of 3 dragons "investing".

There were plenty more interesting presentations and I haven't even touched on any of the fabulous posters so check out the BHIVA website to have a look/listen. Overall it was a great conference so thank you BHIVA, see you again soon!

Harriet Baker
Manchester Foundation Trust

Conference Feedback

International AIDS society (IAS)

International AIDS Society (IAS) conference started in the bustling Mexico City on 21st July with the promise of lots of new data and it did not disappoint at all. The following are a few highlts of the conference as well as the summaries of the different tracks covering basic, clinical, prevention and implementation science.

Dolutegravir and Neural tube defects (NTD)

Dolutegravir (DTG) modelling working group showed that efavirenz (EFV) verse dolutegravir (DTG) with contraception in the efavirenz (EFV) group there are negative benefits in the other clinical outcomes compared to the dolutegravir group.

This work is to be published in New England Journal of Medicine (NEJM).

The Tsepamo study started in August 2014 monitoring the birth outcomes of antiretroviral therapy (ART). DTG was used from the middle of 2016 in Botswana and all potential neural tube defects (NTD) were monitored. NTD is formed by week 6 of the pregnancy before the pregnancy is recognised. Previously 4 out of 426 prevalence 0.4% shown an NTD. In 31st March 2019 women conceived prior to DTG warning 40 weeks before. There was a site expansion from 8 to 18 sites 45% to 72% of sites. Patient characteristics by exposure are all similar with respect to folic acid. Folic acid prescribed prior to conception was not done, also folic acid is not fortified in the food. Since May 2018 an addition 1 NTD of 1275 on patients on DTG. 1 NTD of 3492 patients non-DTG, 0 NTG on 2172 patients on EFV, 1 NTG DTG started in pregnancy. 9 NTD in 23,315 HIV negative women. Overall NTD is lower than in prior years. Higher malformation structural in DTG arm- no prevalence difference. No difference in birth outcomes in DTG vs EFV.

Weight gain with TAF and DTG

NAMSAL trial data patient on tenofovir DF (TDF), tenofovir AF (TAF) and DTG in black people and women as well. Weight gain was seen in treatment naïve patient on DTG or Biktarvy (BTG) in black women especially. Weight loss is seen in patients on TDF based regimen. With the weight gain it is important to note there are clinical implications of obesity in obstetrics – child birth, Type 2 diabetes, cardiovascular disease, mobility to work and short lifespan. NAMSAL cohort saw higher female participates and higher VL at baseline. In the DTG arm 14% male and 12% female saw an increase in weight.

In the ADVANCE trial which compared; TDF +DTG vs TAF+DTG vs TDF+EFV- 96-week study 48-week study presented. This was a predominately female based trial each of the anti-retroviral groups were similar in response the best predictive factor was age and employment. 60% suppressed with young and unemployed and approaching 100% with over 60 years and employed.

Women at week 96 10kg weight gain higher in DTG and higher in TAF arm compared to men which was 5kg weight. In men it there were similar fat and lean muscle gain. In women there were more fat gain over lean muscle.

5 years younger CD4 count higher than NAMSAL female higher BMI and higher mean weight. All 3 arms had an increase in weight significant weight increase especially on TAF.

Progressive rises at week 48 in weight in men in DTG +TAF arm after week 48 it plateaued. 20% of weight gain in men at week 48 and increased obesity. For women conversely the weight gain increased after week 48 and up to week 96. Heat maps shown that there were dramatic increases in the weight for women on TAF+DTG over a period of time.

Changes progressive week 96 16% experienced and moved into this category. Weight increases and obesity increases- week 96 obese category. This was adjusted for socioeconomic graphics, other medications. 10% increase in weight in TAF +DTG. Patient's perceptions of weight gain- no discontinuations. 8 women unhappy, 6 women weight distribution in the abdomen. 2 men weight loss. Follow up participates for two years to find reason and why.

Rapporteur report

The rapporteur report at the end of the conference gave a good summary of the key points in each of the tracks that were presented.

Track A- Basic Science- this summarised that macrophages are long term reservoirs for HIV.

Conference Feedback

as they are long lived and transcriptionally silent which means that they are more hidden by the immune system. Also, they can replenish the memory reservoir by differentiation. They also mention the San Francisco patient who was diagnosed in 1992 and never treated with anti-retroviral medications. They had 24 years of recorded undetectable virus and 34 blood tests that were all below the limits of detection. The following tests were down to show no genome-intact HIV-1 provirus identified, no replication-competent HIV in resting CD4 cells and no intact provirus in resting CD4 cells. Which might show sterilising cure of HIV-1 through natural immunity.

Track B- Clinical Science – much talk was about dolutegravir and neural tube defects (NTDs) and this is mentioned above. It was also discussed about the disadvantages of choosing a non-dolutegravir based regimen. Including increased pre-term delivery with boosted protein inhibitors and more virological failures with an efavirenz based regimen instead. As well as the importance of community engagement with these trials that are being conducted.
GEMINI-2 study showed at week 96 that 3TC+DTG vs TDF/FTC +DTG as first line was non-inferior, also no emergent resistance was seen. The TANGO study showed that 3TC+DTG was a feasible option for a switch regimen where patients were suppressed on a TAF three drug-based regimen. At 48 weeks 3TC+DTG was non-inferior and no emergent resistance was seen as well. New drugs were described including Islatravir (MK8591) first class in nucleoside reverse transcription translocation inhibitor (NRTTI) phase two study as part of the potential 2DR with doravirine.

Track C- Prevention Science - This was the first time that a plenary was dedicated to transgender women especially prevention and continuum in care in Prep. There were a few sessions which identified the issue which transgender women have to deal with including, housing, depression, drugs, poverty and violence. All of which is aggravated by the stigma associated with being transgender. Also, the importance of competent service delivery has a better outcome of care for transgender patients. Also, government involvement is vital as many countries do not recognise their gender identity.
EPIC study run in Australia there was a 44% reduction of HIV incidence 13% stopped Prep for greater than three months and 39.8% restarted. It is thought that they stopped when they were at low risk. A new biomedical prevention Islatravir implant (MK-8591) was discussed. This is similar to Nexplanon were two doses were tested (54mg and 62mg). The higher dose achieved protective concentration for over a year, and it was well tolerated by patients.

Track D- Social, Behavioural and Implementation Science - This was the first year where implementation science and social and behavioural science were married up together. There were sessions which involved the community which helped with programme success. This included involving the community all along, including the designing of the interventions and generating evidence. The DREAMS programme allows women and young girls to be at the centre. There is a core package which empowers women/young girls to reduce risk by strengthening families, reducing risk of sexual partners and mobilising communities for change. They are able to use data to reach key gaps in specific populations and format the inventions needed. This can be applied over different countries and populations.
Community engagement is taken more seriously in clinical trials. The iPrevent study in Cape Town, South Africa. They are engaging the end user in the research process before the product reaches the marketplace. Also, the AMP study experience where early and ongoing experience early and ongoing engagement is proving successful, feasible and being increased. Sawa sawa intervention in Mozambique used mass media, community dialogue and being present as well as changing the minds on the investigators helped reduce stigma. This reduction in the stigma index increased HIV testing in the male participates.

I would like to thank HIVPA for the opportunity to attend this conference as part of the HIVPA bursary, also the support of my colleagues and my family.

Sacha Pires
Barts Heath NHS Trust

HIVPA Sponsors

Promotional material
Dear Pharmacist,
As you are aware, the new tender for generic Atripla and Truvada combinations commenced on the 25th May 2019.

Dr. Reddy's is pleased to announce that we have won the following three regions for the Triple combination efavirenz/emtricitabine/tenofovir disoproxil 600mg/200mg/245mg film coated tablets (Atripla).

Regions won by Dr.Reddy's:
- North Central and North East London
- North West London
- South London

Dr. Reddy's are also delighted to announce that we have also won the following two regions for the double combination emtricitabine/tenofovir disoproxil 200mg/245mg film coated tablets (Truvada).

Regions won by Dr.Reddy's:
- North of England
- South London

Dr Reddy's has also been supplying generic HIV products via national tenders, interim agreements and off contract for the last 4 years, which include the following product:

- Abacavir Lamuvidine
- Darunavir
- Nevirapine
- Tenofovir Mono
- Efavirenz

New Product Launches
We are also looking forward to launching abacavir 300mg film coated tablets into the UK market in July 2019.

Dr. Reddy's is an integrated pharmaceutical company, committed to developing new product launches and providing affordable and innovative medicines for healthier lives.

For customer services please contact: Customerserviceuk@drreddys.com or
John Vaughan Head of Hospitals UK: jvaughan@drreddys.com

A POWERFUL START

Tivicay + lamivudine
dolutegravir

A COMPLETE REGIMEN

AN INNOVATIVE NEW TREATMENT FOR YOUR PATIENTS LIVING WITH HIV

POWERED BY DOLUTEGRAVIR

at the core

DURABLE, NON-INFERIOR EFFICACY WITH 0 RESISTANCE

vs a 3-drug regimen[1]

FEWER ANTIRETROVIRALS VS A 3-DRUG REGIMEN:

TDF, TAF and **ABC free**[2,3]

GEMINI-1 AND GEMINI-2 96-WEEK DATA IN TREATMENT-NAÏVE PATIENTS:

DTG + 3TC 86.0% (N=716) VS DTG + TDF/FTC 89.5% (N=717)[1]

(PROPORTION OF PATIENTS WITH HIV-1 RNA <50 COPIES/ML)

Studied in HBV-negative adult patients with screening viral loads up to 500,000 copies/mL.
Suitable for patients with no known or suspected viral resistance to integrase inhibitors or lamivudine.

References: 1. Cahn P, Sierra Madero J, Arribas J, et al. IAS 2019; Mexico City, Mexico; July 21-24 2019. Presentation WEAB0404LB; **2.** TIVICAY Summary of Product Characteristics. March 2019; **3.** EPIVIR Summary of Product Characteristics. February 2019.

Prescribing Information

Tivicay dolutegravir 10mg, 25mg and 50mg tablets

See Summary of Product Characteristics before prescribing

Indication: HIV in >6 years and ≥15kg as part of combination therapy. **Dosing:** *Adults & adolescents ≥40kg*: 50mg once daily with or without food if no proven/ suspected integrase resistance. Children 6 to <12 years: dose according to bodyweight: 15-<20kg: 20mg once daily (2x10mg); 20-<30kg: 25mg once daily; 30-<40kg: 35mg once daily (1 x 25mg + 1 x 10mg); When co-administered with efavirenz, nevirapine, tipranavir/ritonavir, etravirine (without boosted PI), carbamazepine, oxcarbazepine, phenytoin, phenobarbital, St John's Wort or rifampicin, Tivicay 50mg twice daily in adults/adolescents or the weight-based once daily dose twice daily in paediatric patients. *Adults with proven or suspected integrase resistance:* 50mg twice daily preferably with food. Limited data in paediatric patients with proven/suspected integrase resistance. *Elderly:* Limited data in 65+ yrs. Caution in severe hepatic impairment. **Contraindications:** Hypersensitivity to any ingredient. Co-administration with dofetilide.

Warnings/precautions: Risk of hypersensitivity reactions. Discontinue dolutegravir and other suspect agents immediately if suspected. The two-drug regimen of dolutegravir and lamivudine is only suitable for the treatment of HIV-1 infection where there is no known or suspected resistance to the integrase inhibitor class, or to lamivudine. Risks of osteonecrosis, immune reactivation syndrome. Monitor LFTs in Hepatitis B/C co-infection and ensure effective Hepatitis B therapy. Caution with metformin: monitor renal function and consider metformin dose adjustment. Use with etravirine requires boosted PI or increased dose of dolutegravir. Use with Mg/ Al-containing antacids, calcium, multivitamins or iron requires dosage separation. **Pregnancy/ lactation:** Before initiating dolutegravir, women of childbearing potential (WOCBP) should undergo pregnancy testing. WOCBP who are taking dolutegravir should use effective contraception.

Dolutegravir should not be used during the first trimester due to the potential risk of neural tube defects, unless there is no alternative.

Dolutegravir should only be used during the second and third trimester of pregnancy when the expected benefit justifies the potential risk to the foetus. Avoid breast-feeding. **Side effects:** See SmPC for full details. Headache, GI disturbance, insomnia, abnormal dreams, depression, anxiety, dizziness, rash, pruritus, fatigue, elevations of ALT, AST and CPK, arthralgia, myalgia, hypersensitivity, suicidal ideation or suicide attempt, acute hepatic failure. **Basic NHS costs:** £498.75 for 30 x 50mg tablets EU/1/13/892/001. £99.75 for 30 x 10mg tablets (EU/1/13/892/003). £249.38 for 30 x 25mg tablets (EU/1/13/892/005). MA holder: ViiV Healthcare BV, Huis ter Heideweg 62, 3705 LZ Zeist, Netherlands. Further information available from Customer Contact Centre, GlaxoSmithKline UK Ltd, Stockley Park West, Uxbridge, Middlesex UB11 1BT.

POM S1A

Date of approval: April 2019. PI-1290

Prescribing Information

Epivir - Lamivudine 300mg tablets

See Summary of Product Characteristics (SmPC) before prescribing

Indications: HIV in adults, adolescents and children weighing at least 25 kg as part of combination therapy. **Dose:** Adults: one 300mg tablet daily with or without food. See SmPC for dosage in children and adolescents. Additional formulations available: 150mg tablets and Oral Solution (10mg/mL) – see SmPCs. *Elderly:* No specific data. *Renal impairment*: Creatinine clearance <50ml/min: see SmPC for dosage adjustment. *Hepatic impairment*: no dose adjustment required. **Contraindications:** Hypersensitivity to any ingredient. **Warnings/precautions:** High risk of virological failure (when used in a triple nucleoside regimen), immune reactivation syndrome, osteonecrosis, increased weight, lipids, glucose. Monitor LFTs in Hepatitis B/C co-infection. Use with cladribine, emtricitabine or high doses of co-trimoxazole not recommended. When possible, avoid chronic co-administration of sorbitol or other osmotic acting alcohols (see SmPC section 4.5). If unavoidable, consider more frequent viral load monitoring.

Pregnancy/lactation: Not recommended. Avoid breast-feeding. **Side effects:** See SmPC for full details. Headache, GI disturbance, insomnia, cough, nasal symptoms, rash, alopecia, arthralgia, muscle disorders, fatigue, malaise, fever, blood dyscrasias, pancreatitis, hepatitis, angioedema, rhabdomyolysis, lactic acidosis, peripheral neuropathy. Transient increases in liver enzymes.

Basic NHS costs: 30 tablets: £157.51 EU/1/04/298/002. MA holder: ViiV Healthcare BV, Huis ter Heideweg 62, 3705 LZ Zeist, Netherlands. Further information is available from Customer Contact Centre, GlaxoSmithKline UK Ltd, Stockley Park West, Uxbridge, Middlesex UB11 1BT.

POM S1A

Date of approval: January 2019. Zinc code: UK/3TC/0001/18(1)

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.

Adverse events should be reported. For Ireland, adverse events should be reported directly to the HPRA; Freepost, Pharmacovigilance Section, Health Products Regulatory Authority, Earlsfort Terrace, Dublin 2, Tel: +353 1 676 4971, *medsafety@hpra.ie*. Adverse events should also be reported to GlaxoSmithKline on 1800 244 255.

PM-GB-DLM-ADVT-190002 August 2019

A new option in HIV-1

Make Doravirine▼ a Part of Every Day

DELSTRIGO® (100 mg doravirine/300 mg lamivudine/300 mg tenofovir disoproxil fumarate, equivalent to 245 mg of tenofovir disoproxil) is indicated for the treatment of adults infected with HIV-1 without past or present evidence of resistance to the NNRTI class, lamivudine, or tenofovir.[1]

PIFELTRO® (doravirine) is indicated, in combination with other antiretroviral medicinal products, for the treatment of adults infected with HIV-1 without past or present evidence of resistance to the NNRTI class.[2]

▼ This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions.

PIFELTRO® ▼
Doravirine

DELSTRIGO® ▼
Doravirine/Lamivudine/Tenofovir disoproxil fumarate

PRESCRIBING INFORMATION

Refer to Summary of Product Characteristics (SmPC) before prescribing

Adverse events should be reported. Reporting forms and information can be found at www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store. Adverse events should also be reported to MSD, UK (Tel: 01992 467272).

PRESENTATION: Pifeltro: film-coated tablet containing 100 mg doravirine. **Delstrigo:** film-coated tablet containing 100 mg doravirine, 300 mg lamivudine and 300 mg tenofovir disoproxil fumarate, equivalent to 245 mg of tenofovir disoproxil.

USES: Pifeltro: For use in combination with other antiretrovirals, for the treatment of HIV-1 without past or present evidence of resistance to non-nucleoside reverse transcriptase inhibitors (NNRTI). **Delstrigo:** For the treatment of HIV-1 without past or present evidence of resistance to NNRTIs, lamivudine or tenofovir.

DOSAGE AND ADMINISTRATION: Therapy should be initiated by a physician experienced in HIV infection management. **Pifeltro:** One 100 mg tablet once daily. **Delstrigo:** One 100/300/245 mg tablet once daily. **Pifeltro and Delstrigo:** If co-administered with rifabutin or other moderate CYP3A inducers, increase doravirine dose to 100 mg twice daily (12 hours apart). **Pifeltro:** *Elderly:* No dose adjustment necessary. *Renal impairment:* No dose adjustment necessary. *Hepatic impairment:* mild to moderate: no dosage adjustment required; severe: use with caution. **Delstrigo:** *Elderly:* Special care advised. *Renal impairment:* estimated creatinine clearance (CrCl) ≥50 mL/min: no dose adjustment necessary; estimated CrCl <50 mL/min: not recommended. *Hepatic impairment:* mild to moderate: no adjustment required; severe hepatic: use with caution.

CONTRA-INDICATIONS: Hypersensitivity to the active substance or excipients Co-administration with strong CYP3A inducers.

PRECAUTIONS: A residual risk of sexual transmission of HIV-1 cannot be excluded and precautions should be taken in accordance with national guidelines. Use with CYP3A inducers may reduce the exposure of doravirine. Autoimmune disorders and immune reactivation syndrome have been reported in patients treated with combination antiretroviral therapy which may require investigation and treatment. Contains lactose monohydrate. **Delstrigo:** Post-treatment exacerbation of HBV (including hepatic decompensation and liver failure) have been reported in patients co-infected with HIV-1 and HBV following discontinuation of lamivudine or tenofovir disoproxil. Monitor patients co-infected with HIV-1 and HBV after discontinuation of Delstrigo and if appropriate initiate anti-HBV therapy. Renal impairment, including acute renal failure and Fanconi syndrome have been reported with tenofovir disoproxil. Assess estimated CrCl prior to initiation and during therapy. In patients at risk of renal dysfunction, serum phosphorus, urine glucose, and urine protein should also be assessed. Discontinue therapy if estimated CrCl declines below 50 mL/min. Avoid with concurrent or recent use of nephrotoxic medicinal products (e.g. high-dose or multiple NSAIDs). Evaluation of renal function is recommended for persistent or worsening bone pain, pain in extremities, fractures, and/or muscular pain or weakness. Assessment of bone mineral density should be considered for patients who have a history of pathologic bone fracture or other risk factors for osteoporosis or bone loss. Hypophosphatemia and osteomalacia secondary to proximal renal tubulopathy should be considered in patients at risk of renal dysfunction who present with persistent or worsening bone or muscle symptoms. Doravirine/lamivudine/tenofovir disoproxil must not be co-administered with other medicinal products containing lamivudine, tenofovir disoproxil, or tenofovir alafenamide or with adefovir dipivoxil. Doravirine/lamivudine/tenofovir disoproxil should not be administered with doravirine unless needed for dose adjustment (e.g. co-administered with rifabutin). **Drug interactions:** Refer to SmPC for full information on drug interactions. **Pifeltro and Delstrigo:** Doravirine is metabolized primarily by CYP3A. Do not co-administer with strong CYP3A enzyme inducers. If co-administeration with rifabutin or other moderate CYP3A inducers cannot be avoided, increase doravirine dose to 100 mg twice daily (taken 12 hours apart). Use with caution when co-administering doravirine with medicinal products that are sensitive CYP3A substrates that have a narrow therapeutic window (e.g., midazolam, tacrolimus and sirolimus). **Delstrigo:** Do not administer with other antiretroviral medicinal products. Co-administration of doravirine/lamivudine/tenofovir disoproxil with medicinal products that reduce renal function or compete for active tubular secretion may increase serum concentrations of lamivudine. Co-administration of doravirine/lamivudine/tenofovir disoproxil with medicinal products that reduce renal function or compete for active tubular secretion via OAT1, OAT3 or MRP4 may increase serum concentrations of tenofovir. Avoid with concurrent or recent use of nephrotoxic medicinal products. **Pregnancy and Lactation: Pifeltro and Delstrigo:** Avoid use during pregnancy. An Antiretroviral Pregnancy Registry has been established. Breastfeeding is not recommended.

SIDE EFFECTS: Refer to SmPC for complete information on side-effects. **Pifeltro and Delstrigo:** ***Common:*** abnormal dreams, insomnia, headache, dizziness, somnolence, nausea, diarrhoea, abdominal pain, vomiting, rash, fatigue, flatulence, increased alanine aminotransferase. ***Uncommon:*** depression, hypophosphataemia, suicidal ideation, paraesthesia, asthenia. ***Rare:*** rash pustular, hypomagnesaemia, aggression, hallucination, dyspnoea, acute kidney injury, renal disorder, calculus urinary, nephrolithiasis, chest pain. **Delstrigo:** ***Common:*** cough, nasal symptoms, alopecia, muscle disorders, fever. ***Uncommon:*** neutropenia, anaemia, thrombocytopenia, pancreatitis, rhabdomyolysis, proximal renal tubulopathy (including Fanconi syndrome). ***Rare:*** lactic acidosis, hepatitis, angioedema, myopathy, acute renal failure, renal failure, acute tubular necrosis, nephritis (including acute interstitial) and nephrogenic diabetes insipidus. ***Very Rare:*** pure red cell aplasia, peripheral neuropathy (or paraesthesia).

PACKAGE QUANTITIES AND BASIC NHS COST:
Pifeltro: Bottle of 30 tablets £471.41
Delstrigo: Bottle of 30 tablets £578.55

MARKETING AUTHORISATION NUMBER
Pifeltro: EU/1/18/1332/001
Delstrigo: EU/1/18/1333/001

MARKETING AUTHORISATION HOLDER
Merck Sharp & Dohme B.V.
Waarderweg 39
2031 BN Haarlem
The Netherlands

Legal Category: POM

Date of review of prescribing information: April 2019

PI.PIF-DEL.19.UK.6791.II-001

REFERENCES:
1. DELSTRIGO Summary of Product Characteristics.
2. PIFELTRO Summary of Product Characteristics.

MSD

Merck Sharp & Dohme Limited. Registered Office Hertford Road, Hoddesdon, Hertfordshire EN11 9BU Registered in England No. 820771

Doravirine▼ SmPC Overview

Pifeltro ▼(doravirine) and Delstrigo ▼(doravirine/lamivudine/tenofovir disoproxil fumurate)
UK Prescribing Information and Adverse Event Reporting please click here
For those HIVPA members based in Ireland for prescribing information please click here

Doravirine SmPC update

As you may be aware, doravirine received a marketing authorisation at the end of November 2018. The purpose of this bulletin is to provide an update of the Summary of Product Characteristics (SmPC) of doravirine single entity tablet and the combination tablet.

Doravirine is a non-nucleoside reverse transcriptase inhibitor (NNRTI) that exists as either a white single entity tablet of 100 mg doravirine (DOR), or as a yellow combination tablet (DOR/3TC/TDF)* of 100 mg doravirine with 300 mg lamivudine (3TC) and 300 mg tenofovir disoproxil fumarate (TDF).

Indication

DOR is indicated in combination with other antiretroviral medicinal products for the treatment of adults infected with HIV-1 without past or present evidence of viral resistance to the NNRTI class. In contrast, the DOR/3TC/TDF is indicated for the treatment of adults infected with HIV-1 without past or present evidence of viral resistance to the NNRTI class, lamivudine, or tenofovir.

Both are administered orally, one tablet once daily, without regard to food. A dose adjustment is required if the either tablet is administered with rifabutin, or other moderate CYP3A inducers. At this point, doravirine would need to be adjusted to 100 mg twice daily (BiD) 12 hours apart.

Metabolism and elimination

Doravirine is primarily metabolised by oxidative metabolism via cytochrome P450 3A (CYP3A) in the liver. Lamivudine and tenofovir disoproxil fumarate are eliminated via glomerular filtration and active tubular secretion.

Contraindications

Both tablets are contraindicated for patients with hypersensitivity to the active substance or excipients (note that both tablets contain lactose) and when co-administered with strong CYP3A inducers such as rifampicin, due to the drug-drug interaction with doravirine. Patients with a creatinine clearance (CrCl) less than 50mL/min should not receive the combination tablet (DOR/3TC/TDF) as the necessary dosage adjustments for 3TC and TDF cannot be made.

Drug-drug interactions

DOR and DOR/3TC/TDF are contraindicated for patients on strong CYP3A inducers. However, whilst CYP3A inhibitors may result in increased doravirine concentrations, no dose adjustment is required. Whilst doravirine is not likely to have a clinically relevant effect on drugs dependent of CYP enzymes, caution is advised when co-administering DOR or DOR/3TC/TDF with narrow therapeutic window medications dependent on CYP enzymes. No dose adjustment is required when doravirine is administered with a proton pump inhibitor (PPI) or an oral contraceptive. A full list of the interactions for both tablets is listed on the Liverpool Drugs Website: www.hiv-druginteractions.org

Trials

Two treatment naïve (DRIVE-FORWARD and DRIVE-AHEAD) have supported the launch of DOR and DOR/3TC/TDF. Both trials met their primary endpoint; proportion of patients with a HIV-1 viral RNA <50 copies/mL using FDA snapshot approach. DRIVE-FORWARD compared DOR +2NRTIs vs ritonavir-boosted darunavir (DRV+r) + 2NRTIs. DRIVE-AHEAD compared DOR/3TC/TDF vs EFV/FTC/TDF**. Lower incidences of dizziness and abnormal dreams were seen vs EFV/FTC/TDF in DRIVE-AHEAD and comparable incidences of dizziness between the arms were seen in DRIVE-FORWARD. Headache and nausea were the most common adverse events seen in the trials. At 96 weeks, 10/747 participants from the treatment naïve trials developed genotypic resistance to doravirine.

Adverse events should be reported. Reporting forms and information can be found at www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store. Adverse events should also be reported to MSD, UK (Tel: 01992 467272).

*DOR/3TC/TDF = Doravirine/Lamivudine/Tenofovir Disoproxil Fumarate
**EFV/FTC/TDF = Efavirenz/Emtricitabine/Tenofovir Disoproxil Fumarate

Please refer to SmPC for detailed prescribing information

Doravirine 100 mg: https://www.medicines.org.uk/emc/product/9693/smpc
DOR/3TC/TDF 100 mg/300 mg/300 mg: https://www.medicines.org.uk/emc/product/9694/smpc

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