"Managing HIV and Cancer Care: A 38-year old man with non-healing wound following circumcision"

Tuesday, October 20, 2020

BOTSOGO

BOTSWANA ONCOLOGY GLOBAL OUTREACH

Continuing Medical Education Announcement

Harvard Medical School

RSS 3081: Monthly BOTSOGO Tumor Board; 2020 - 2021 Academic Year

Today's Objectives:

- Describe the need for timely cancer case presentation and referral to treatment
- Formulate a multi-disciplinary plan for the care of common and complex oncologic cases
- Adopt successful, sustainable strategies to mitigate barriers to quality cancer care common in resource constrained environments

Target Audience:

Oncologists, internists, surgeons, radiation oncologists, infectious disease specialists, nurses, physicists, therapists, technicians, research staff, administrators, policy makers.

Financial Relationships

The following planners, speakers, and content reviewers, on behalf of themselves and their spouse or partner, have reported financial relationships with an entity producing, marketing, re-selling, or distributing health care goods or services (relevant to the content of the activity) consumed by, or used on, patients:

Name	Role	Type of Financial Relationship
Jason Efstathiou, MD	Course Director	Blue Earth Diagnostics – Consultant Taris Biomedical – Consultant Janssen – Advisory Board
Bruce Chabner, MD	Course Planner	EMD Serono – Consultant Chagai - Consultant Boston Pharmaceutical – Consultant Eli Lilly – Consultant Takeda Pharmaceuticals – Consultant Bristol Myers Squibb – Lecture Honoraria Alnylam Pharmaceuticals – Equity Holding Abbott Laboratories – Equity Holding Bluebird – Equity Holding Biomarin – Equity Holding Constellation Pharmaceuticals – Equity Holding Glaxo Smith Klein – Equity Holding PharmaMar – Equity Holding Seattle Genetics – Equity Holding Springworks – Equity Holding

Financial Relationships *(continued)*

The following planners, speakers, and content reviewers, on behalf of themselves and their spouse or partner, have reported financial relationships with an entity producing, marketing, re-selling, or distributing health care goods or services (relevant to the content of the activity) consumed by, or used on, patients:

Name	Role	Type of Financial Relationship
Peter Vuylsteke, MD	Course Planner	Novartis – Consultant Pfizer – Consultant Lilly – Consultant MSD – Consultant, Travel grants AstraZeneca – Consultant, Travel grants Roche – Consultant, Travel grants

All other individuals including course directors, planners, reviewers, faculty, staff, etc., who are in a position to control the content of this educational activity have reported no financial relationships related to the content of this activity.

Financial Relationships *(continued)*

All other individuals including course directors, planners, reviewers, faculty, staff, etc., who are in a position to control the content of this educational activity have reported no financial relationships related to the content of this activity.

Statements

Accreditation Statement

The Harvard Medical School is accredited by the Accreditation Council for Continuing Medical Education to provide continuing medical education for physicians

Credit Designation Statement

The Harvard Medical School designates this live activity for a maximum of 1 *AMA PRA Category 1 Credit™*. Physicians should claim only the credit commensurate with the extent of their participation in the activity

This activity meets the criteria of the Massachusetts Board of Registration in Medicine for 1.0 credits of Risk Management Study

Disclosure Statement

In accord with the disclosure policy of the Medical School as well as standards set forth by the Accreditation Council for Continuing Medical Education, course planners, speakers, and content reviewers have been asked to disclose any relevant relationship they, or their spouse or partner, have to companies producing, marketing, re-selling or distributing health care goods or services consumed by, or used on, patients.

Claim your CME credits!

- To claim your CME credit for attendance at this session of the BOTSOGO Tumor Board, please fill out our survey following the Tumor Board.
- You can do this at your convenience on your personal or work computer by navigating to www.botsogo.org
  - Click “What We Do”
  - Click “Tumor Board”
  - Click the link under the section “Continuing Education Credits,” and complete and submit the survey
- A link to the survey is also sent to the BOTSOGO Tumor Board email list following each Tumor Board.

Core Principles of Case Review

Clinicians, pathologists, and other other members of the health care team uniformly strive to provide the best possible clinical care.

Despite these efforts, adverse outcomes still occur.

Reflection on, and re-evaluation of, our practices and outcomes are imperative to continuously improve the care we provide to patients.

Core Principles of Case Review

Discussion will focus on medical decision-making and reporting systems.

Discussion is privileged and content should not be discussed outside of this forum.

We seek to create a safe, collaborative, open and respectful atmosphere for discussion, learning, and improvement

Faculty, October 20, 2020

Peter Vuylsteke, MD

University of Botswana; Princess Marina Hospital

Sebathu Chiyapo, MD

Gaborone Private Hospital

Rick Lee, MD, PhD

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MGH Department of Urology

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MGH Department of Radiation Oncology

COVID STATS IN BOTSWANA

Peter Vuylsteke, MD

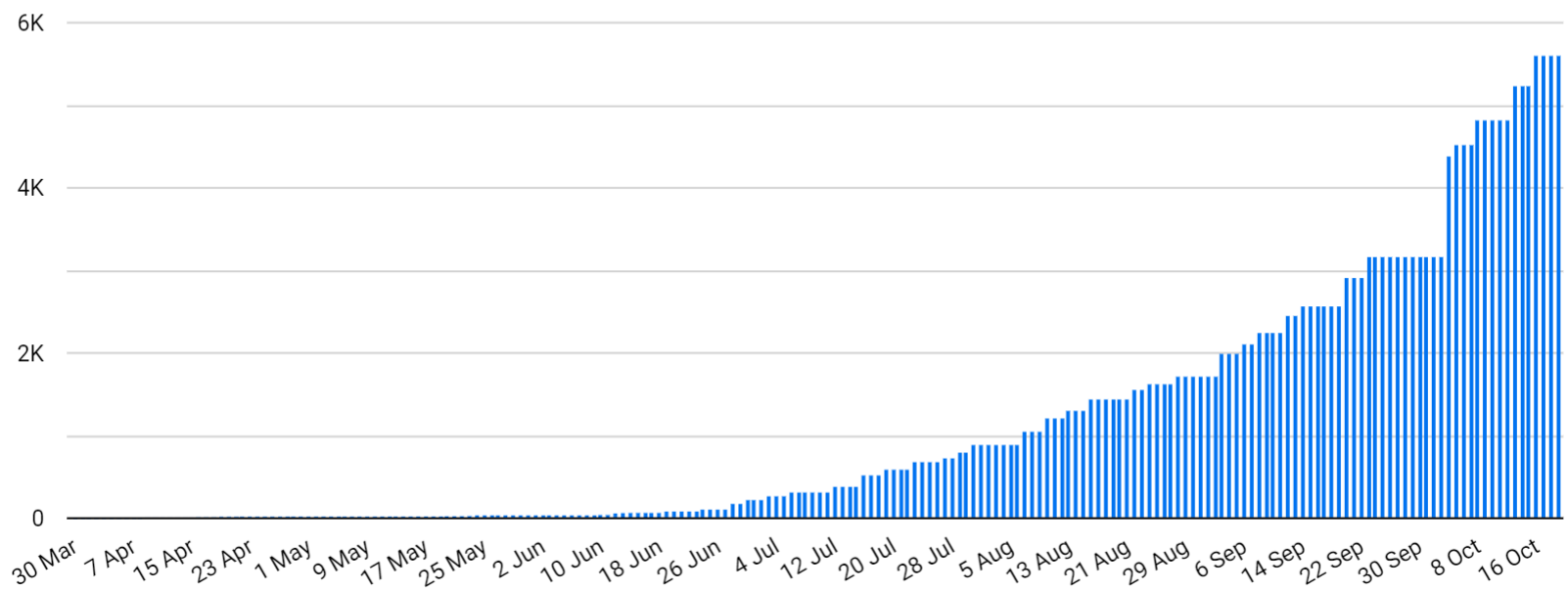
BOTSOGO

BOTSWANA ONCOLOGY
GLOBAL OUTREACH

Total Cases	Local Cases	Local Fatalities	Local Active	Local Recoveries
5,609	4,274	21	3,338	915
Since 30/03/2020 till present.	Transfered Out	Total Tests	Border Tests	Local Tests
	1,335	267,517	99,166	168,351

Confirmed Cases

Cumulative Confirmed Cases



Measures

Mandatory wearing of masks everywhere

BW Borders closed

Register of entries

Active Contact tracing

Hospital PMH: Biweekly staff swab screening

Cancer patients:

- COVID test on admission
- No repeated COVID tests on CHEMO-ward

"Managing HIV and Cancer Care:
A 38-year old man with non-healing wound following circumcision"

Isaac Nkele

Dr Dickenson

Dr Tyreman

Case

Mr X

38 year-old male
HIV+ve on HAART salvage line (dtg+truvada+dart+rit) with non-healing ulcer on penis.

Past Medical History:
Treatment for pulmonary tuberculosis in 2014- completed tx.

HAART History

- HIV +ve since 2010 and started HAART in 2010 on Atripla.
- Hx of defaulting tx which patient attributes to work stressors.
- 2015 VL 850 CD4 188
- 2016 patient was not virally suppressed so switched to CBV+ Alluvia.
- Patient was reportedly having unresolving diarrhea since switch.

HAART hx Continued…

2016 Was then switched to CBV+ATEZANAVIR+Ritonavir about a month later.

Mid-2017: cd4 290

Late 2017: cd4 195, viral load 77791

Early 2018: -Cd4 113(13.25%)

Mid 2018: VL 22638

Early 2019: Cd4 235(15%)

Early-mid 2019: VL <400

- Early 2019: Pt seen by HIV specialist; documented drug resistance to all other PIs. Plan salvage treatment with:

  Darunavir 600mg+Ritonavir 100mg in addition to DTG & TRU.

Patient history

PSHx

- Circumcision was done in 2017.

Medical History

- HAART

Family History

- Nil Significant hx

Social History

- Married with one child.
- holds a tertiary qualification in carpentry, but currently unemployed
    - Alcohol: former drinker
    - Smoking: Ex-smoker

HPC

Circumcision done in 2017. Patient reported penile ulcer that would not heal for several months despite being seen several times at healthcare facility for wound cleaning and dressing.

Patient was seen in Urology clinic and biopsy was done in early 2018.

PATHOLOGY REPORT:
Revealed - invasive moderately differentiated SCC in a background of condyloma acuminatum w/ high-grade penile intraepithelial neoplasia.

PMH ONCOLOGY VISIT

Patient was then referred to Oncology in late 2018.

Penectomy was advised but patient declined since no possibility of doing penis reconstruction in Botswana and instead opted for different tx options.

Patient booked for early 2019. Significant clinical findings on visit exam:

ECOG –PS 1, Pain- 5/7

Penile mass involving the glands and shaft invading the corpora cavernosa, palpable mass 3x2cm and mobile.

Clinically staged T3N2MX=stage3b

Management plan

If no mets: neoadjuvant chemo-surgery-rt

If mets: palliative chemo

Staging investigations:
Chest X-Ray
Abd ultrasound
CT chest and abdomen

Investigations

- CT chest and abdomen findings (Early 2019)
  No mass lesion shown in the chest and abdomen, bilateral hydrocele both scrotal sacs, few enlarged lymph nodes both inguinal, no ascites
- Bloods (Early 2020)
  RFTS, LFTS, FBC normal
- Abdominal and pelvic ultrasound (mid-2020)
  Inflamed and enlarged lymph node(left iliac fossa)
  Bowel mass

Staging

Penile cancer stage IV

ONCOLOGY VISIT #1 (mid-2020)

Presenting with bilateral ulcer-inguinal lymph nodes

Bloods- normal

Plan: palliative chemotherapy

Chemo-docetaxel, and carboplatin

NRH ONCOLOGY VISIT #2 (mid-2020)

Six cycles-palliative treatment with

Paclitaxel(230mg)

Carboplatin(450mg)

Completed six chemo cycles in mid-late 2020

Report reduction in smell and the wound size

Discussion

1. Delays in cancer management.
2. Importance and type of multidisciplinary teams for this case
3. How can adherence be emphasized?
4. When should art be switched if poor adherence is identified?
5. When should priority viral load be ordered?
6. Is there any drug interactions that might have caused poor viral suppression?
7. What is the next management step after completion of six chemo cycles.
8. Is partial penectomy an option?

Appendix – Interaction Report

www.hiv-druginteractions.org

UNIVERSITY OF LIVERPOOL

Interaction Report

Report ID:
Date Produced: 20 October 2020

Antiretroviral Treatment	Co-medications
Darunavir + ritonavir (DRV/r)	Carboplatin
Dolutegravir (DTG)	Cisplatin
Emtricitabine/Tenofovir-DF (FTC/TDF, PrEP)	Docetaxel
	Paclitaxel
	Prednisone

This report lists the summaries of potential interactions (i.e. "red", "amber" and “yellow” classifications) for the drugs in the table above.

Interactions with a "green" or "grey" classification (i.e. no clinically significant interaction or no clear data) have been checked and are listed at the end of this report, but summaries are not shown.

For full details of all interactions, see www.hiv-druginteractions.org .

Description of the interactions

Potential clinically significant interaction - likely to require additional monitoring, alteration of drug dosage or timing of administration (AMBER)

Dolutegravir (DTG) + Paclitaxel

Coadministration has not been studied. Paclitaxel is primarily metabolized by CYP2C8 and to a lesser extent by CYP3A4. In vitro data suggest that paclitaxel activates PXR and therefore could potentially decrease dolutegravir concentrations via induction of UGT1A1. Monitor response to antiretroviral therapy.

Emtricitabine/Tenofovir-DF (FTC/TDF, PrEP) + Carboplatin

Coadministration has not been studied. Carboplatin is excreted primarily by renal glomerular filtration and there is little potential for competition for active renal elimination mechanisms by carboplatin, emtricitabine and tenofovir. However carboplatin has nephrotoxic potential and use of tenofovir-DF should be avoided with concurrent or recent use of a nephrotoxic medicinal product. If coadministration is unavoidable, renal function should be monitored closely.

Emtricitabine/Tenofovir-DF (FTC/TDF, PrEP) + Cisplatin

Coadministration has not been studied. Cisplatin is eliminated renally via OCT2 and MATE1: cisplatin and emtricitabine could potentially compete for MATE1, slowing their elimination. Based on metabolism and clearance a pharmacokinetic interaction is unlikely with tenofovir as it is eliminated by other renal transporters, however, coadministration may increase the risk of nephrotoxicity. If coadministration of emtricitabine/tenofovir-DF and cisplatin is necessary, close monitoring of renal function is recommended.

Darunavir + ritonavir (DRV/r) + Cisplatin
Coadministration has not been studied. Cisplatin is eliminated renally via OCT2 and MATE1 and in vitro data indicate that ritonavir is a moderate inhibitor of MATE1. Ritonavir could potentially slow down cisplatin renal elimination and thus increase the risk of nephrotoxicity. Close monitoring of renal function is recommended.

Darunavir + ritonavir (DRV/r) + Docetaxel
Coadministration with darunavir/ritonavir has not been studied. Coadministration with ritonavir may increase concentrations of docetaxel and increase the risk of severe toxicities. There have been several case reports of severe haematological and cutaneous toxicity when coadministered with ritonavir, a potent CYP3A inhibitor. Ideally avoid coadministration with boosted protease inhibitors or consider using an alternative taxane.

Darunavir + ritonavir (DRV/r) + Paclitaxel
Coadministration has not been studied. Paclitaxel is primarily metabolized by CYP2C8 and to a lesser extent by CYP3A4. Ritonavir dosed as a pharmacokinetic booster is a weak inhibitor of CYP2C8 but a strong inhibitor of CYP3A4. Darunavir/ritonavir could potentially increase paclitaxel exposure. However, the European product label for darunavir/ritonavir states that coadministration may decrease concentrations of paclitaxel which could decrease or shorten its therapeutic effect. As it is unclear whether paclitaxel exposure will increase or decrease, monitoring for paclitaxel induced toxicity and of therapeutic effect is recommended.

Darunavir + ritonavir (DRV/r) + Prednisone
Coadministration has not been studied. Prednisone is converted to the active metabolite prednisolone by 11-B-hydroxydehydrogenase. Prednisolone is then metabolized by CYP3A4. Coadministration could potentially increase prednisolone concentrations thus increasing the risk of steroid related toxicity. Careful monitoring for adverse effects is recommended.

No clinically significant interaction expected (GREEN)

Dolutegravir (DTG) + Carboplatin

Dolutegravir (DTG) + Cisplatin

Dolutegravir (DTG) + Docetaxel

Dolutegravir (DTG) + Prednisone

Emtricitabine/Tenofovir-DF (FTC/TDF, PrEP) + Docetaxel

Emtricitabine/Tenofovir-DF (FTC/TDF, PrEP) + Paclitaxel

Emtricitabine/Tenofovir-DF (FTC/TDF, PrEP) + Prednisone

Darunavir + ritonavir (DRV/r) + Carboplatin

Thank you.