RUTGERS
THE STATE UNIVERSITY OF NEW JERSEY

Perinatal HIV Exposure: Antiretroviral Management

Danielle McDonald, PharmD
PGY-2 Pediatric Pharmacotherapy Resident

A presentation for HealthTrust Members
June 1, 2018

Learning Objectives for Pharmacists

- Identify key components of preventing HIV transmission from mother to infant
- Analyze pivotal trials that established the standard of care for intrapartum and postpartum HIV prophylaxis
- Compare infant antiretroviral prophylaxis regimens in regards to efficacy and safety profiles

Learning Objectives for Pharmacy Techs

- List risk factors that increase transmission of HIV from mother to infant
- Identify neonatal HIV medications that are classified as hazardous drugs
- Implement National Institute for Occupational Safety and Health strategies to handle hazardous medications

Disclosures

- This program may contain the mention of drugs or brands presented in a case study or comparative format using evidence-based research. Such examples are intended for educational and informational purposes and should not be perceived as an endorsement of any particular supplier, brand or drug.

- The presenter has no financial relationship with any commercial interests pertinent to this presentation.

Presentation

- 3750 gram, full-term baby girl born to a 39-year-old mother with HIV-1

- Day 1 HIV-1 RNA: Undetected

Maternal History

- Diagnosed three months prior in Kenya; arrived in the United States two months prior to delivery
- Did not receive antiretroviral therapy until admission for delivery
- Underwent elective cesarean delivery
  - Zidovudine 2 mg/kg IV x 1 then 1 mg/kg/hour continuous infusion, initiation three hours prior to cesarean delivery
  - HIV-1 differentiation +
  - CD4 = 268 cell/mcL; HIV-1 RNA 18,072 copies/mL
- Social history: No other children, single

Medication Administration

- Day 1
  - Vitamin K 1 mg IM once
  - Erythromycin ophthalmic ointment 0.5% to each eye once
  - Pediatric hepatitis B vaccine 0.5 mL IM once

	Day	1	2	3	4	5	6	7	8
Zidovudine 4 mg/kg (15 mg) PO q12h	AM		✓	✓	✓	✓	✓	✓	✓
	PM	✓	✓	✓	✓	✓	✓	✓	✓
Nevirapine 12 mg PO			✓						
Lamivudine 2 mg/kg (7.5 mg) PO q12h	AM			✓	✓	✓	✓	✓	✓
	PM		✓	✓	✓	✓	✓	✓	✓
Nevirapine 6 mg/kg (22 mg) PO q12h	AM				✓	✓	✓	✓	✓
	PM			✓	✓	✓	✓	✓	✓

- Day 4 HIV DNA/RNA PCR: pending

HIV and Pregnancy

- 1994 → 2013: Incidence per 100,000 live births decreased from 32 → 1.8 in the United States
  - Universal prenatal HIV counseling and testing
  - Antiretroviral (ARV) prophylaxis
  - Scheduled cesarean delivery
  - Avoidance of breastfeeding

- Critical to maximally suppress viral replication as early as possible during pregnancy
  - Optimize virologic suppression
  - Minimize potential adverse effects

Sources: Panel on Treatment of Pregnant Women with HIV Infection and Prevention of Perinatal Transmission. Available at http://aidsinfo.nih.gov/contentfiles/lvguidelines/PerinatalGL.pdf. Accessed Jan. 30 2018.
Nesheim SR, et al. *J Acquir Immune Defic Syndr*. 2017;76:461-464.

Risks Factors for Transmission

- Cigarette smoking
- Illicit drug use
- Genital tract infections
- Unprotected sexual intercourse with multiple partners during pregnancy
- Acute or recent HIV infection during pregnancy and breastfeeding

NOTE: Most perinatal transmission events occur late in pregnancy or during delivery

Source: Panel on Treatment of Pregnant Women with HIV Infection and Prevention of Perinatal Transmission. Available at http://aidsinfo.nih.gov/contentfiles/lvguidelines/PerinatalGL.pdf. Accessed Jan. 30 2018.

Initial Testing for HIV

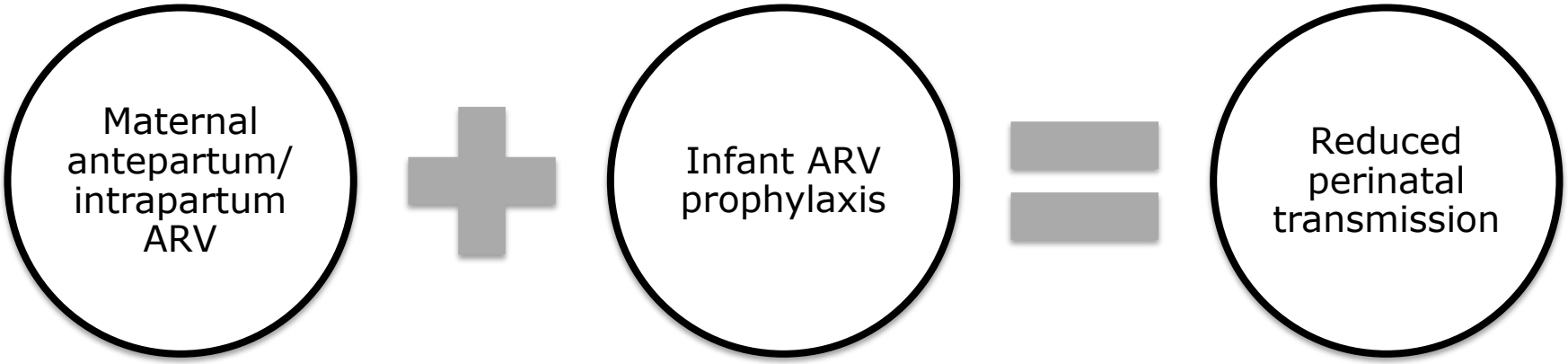
- FDA-approved antigen/antibody combination immunoassay
  - HIV-1 antibodies
  - HIV-2 antibodies
  - HIV-1 p24 antigen

- Positive antigen/antibody tests → type-specific antibody differentiation assay
  - Negative antibody differentiation assay → HIV nucleic acid testing

- Positive HIV nucleic acid testing → confirms **acute** infection
  - Serologic testing within three months for virologic test-positive, antibody-negative individuals

Source: Panel on Treatment of Pregnant Women with HIV Infection and Prevention of Perinatal Transmission. Available at http://aidsinfo.nih.gov/contentfiles/lvguidelines/PerinatalGL.pdf. Accessed Jan. 30 2018.

General Recommendations



Source: Panel on Treatment of Pregnant Women with HIV Infection and Prevention of Perinatal Transmission. Available at http://aidsinfo.nih.gov/contentfiles/lvguidelines/PerinatalGL.pdf. Accessed Jan. 30 2018.

cART in Pregnant Women

- cART with at least **three** agents is recommended

- In general, women should continue their regimens; Exceptions:
  - Didanosine
  - Stavudine
  - Treatment-dose ritonavir

- ARV-naïve pregnant women
  - Preferred regimen: Two nucleoside reverse transcriptase inhibitors (NRTIs) + ritonavir-boosted protease inhibitor or an integrase inhibitor

Source: Panel on Treatment of Pregnant Women with HIV Infection and Prevention of Perinatal Transmission. Available at http://aidsinfo.nih.gov/contentfiles/lvguidelines/PerinatalGL.pdf. Accessed Jan. 30 2018.

Teratogenicity With ARVs

- Antiretroviral Pregnancy Registry (01/01/1989 – 01/31/2017)

ARV Exposure	Number of Outcomes with Defects/Live Births
First-Trimester	240/8583 (2.8%)
Second-/Third-Trimester	254/9220 (2.8%)
Efavirenz	22/978 (2.2%)

- Efavirenz: Previously not recommended before eight weeks gestational age; no longer restricted

- Other considerations:
  - Maternal folate use, folate levels, or folate antagonists
  - Maternal tobacco and alcohol use

Sources: Antiretroviral Pregnancy Registry Steering Committee. Antiretroviral Pregnancy Registry international interim report for 1 January 1989-31 January 2017. Wilmington, NC: Registry Coordinating Center. 2017. Available at http://www.apregistry.com/,
Panel on Treatment of Pregnant Women with HIV Infection and Prevention of Perinatal Transmission. Available at http://aidsinfo.nih.gov/contentfiles/lvguidelines/PerinatalGL.pdf. Accessed Jan. 30 2018.

NRTIs and Pregnancy

	Advantages	Concerns
Preferred Regimens		
Abacavir + lamivudine	• Once-daily dosing • Well-tolerated in pregnancy	• Testing for HLA-B*5701 allele should be performed
Tenofovir disoproxil fumarate (TDF) + emtricitabine or lamivudine	• Once-daily dosing • Well-tolerated in pregnancy • Enhanced activity against hepatitis B	• Bone and growth abnormalities in infants exposed to TDF *In utero* • Renal insufficiency
Alternative Regimen		
Zidovudine + lamivudine		• Insufficient data • Twice-daily dosing • Adverse effects

Source: Panel on Treatment of Pregnant Women with HIV Infection and Prevention of Perinatal Transmission. Available at http://aidsinfo.nih.gov/contentfiles/lvguidelines/PerinatalGL.pdf. Accessed Jan. 30 2018.

PIs and Pregnancy

	Advantages	Concerns
Preferred Regimens		
Atazanavir + ritonavir	• Once-daily dosing • Well-tolerated in pregnancy	• Unclear effect on infant bilirubin levels
Darunavir + ritonavir	• Well-tolerated in pregnancy	• Twice-daily dosing in pregnancy
Alternative Regimen		
Lopinavir + ritonavir		• Twice-daily dosing • Nausea/diarrhea

Source: Panel on Treatment of Pregnant Women with HIV Infection and Prevention of Perinatal Transmission. Available at http://aidsinfo.nih.gov/contentfiles/lvguidelines/PerinatalGL.pdf. Accessed Jan. 30 2018.

Integrase Inhibitors and Pregnancy

- Raltegravir: Preferred agent
  - Non-pregnant adults: More rapid viral decay compared to efavirenz
    - No comparative data in pregnancy
    - Case reports of elevated liver transaminases in late pregnancy
  - Readily crosses placenta → competes with bilirubin for albumin binding sites (unlikely to be clinically significant)
  - Twice-daily dosing
  - Caution: Not recommended in acute infection during pregnancy unless combined with a boosted PI
- Limited data: dolutegravir
- Not recommended: elvitegravir/cobicstat

Source: Panel on Treatment of Pregnant Women with HIV Infection and Prevention of Perinatal Transmission. Available at http://aidsinfo.nih.gov/contentfiles/lvguidelines/PerinatalGL.pdf. Accessed Jan. 30 2018.

Learning Assessment Q #1

Which of the following is true regarding prenatal management of mothers infected with HIV?

A. Combination antiretroviral therapy with at least three agents is recommended

B. Efavirenz should NOT be administered during the first trimester

C. Didanosine should NOT be continued during pregnancy

D. Both A & C

E. All of the above

Assessment Response #1

Which of the following is true regarding prenatal management of mothers infected with HIV?

A. Combination antiretroviral therapy with at least three agents is recommended

B. Efavirenz should NOT be administered during the first trimester

C. Didanosine should NOT be continued during pregnancy

D. Both A & C

E. All of the above

Intrapartum Care

- Continue antepartum combination antiretroviral therapy (cART) on schedule

- HIV RNA > 1,000 copies/mL (or unknown)
  - IV zidovudine (ZDV) near delivery
  - Scheduled cesarean delivery at 38 weeks' gestation

- Unknown HIV status and in labor
  - Expedited antigen/antibody HIV testing → if positive:
    - HIV-1/HIV-2 antibody differentiation test
    - Maternal IV ZDV + infant combination ARV prophylaxis
  - Differentiation test negative + negative HIV RNA test → stop maternal and infant ARV drugs

Source: Panel on Treatment of Pregnant Women with HIV Infection and Prevention of Perinatal Transmission. Available at http://aidsinfo.nih.gov/contentfiles/lvguidelines/PerinatalGL.pdf. Accessed Jan. 30 2018.

Why Zidovudine?

- Reduction of maternal HIV viral load
- Crosses the placenta readily
- High cord-to-maternal blood ratio
- Penetrates the central nervous system
- Metabolized to active triphosphate within the placenta
  - May provide additional protection against transmission
  - Not observed with other nucleoside analogues
- Only wild-type virus appears to be transmitted from mother to infant

Source: Panel on Treatment of Pregnant Women with HIV Infection and Prevention of Perinatal Transmission. Available at http://aidsinfo.nih.gov/contentfiles/lvguidelines/PerinatalGL.pdf. Accessed Jan. 30 2018.

IV ZDV During Labor

- Additional benefit of IV ZDV in women receiving cART has not been evaluated in randomized clinical trials

- Based on observational studies, IV ZDV is not required for HIV-infected women receiving ART with HIV RNA ≤ 50 copies/mL near delivery
  - **NOTE**: Inadequate data to determine administration of IV ZDV if HIV RNA in the range of 50 to 999 copies/mL

- IV ZDV should begin **three hours** before cesarean delivery

Source: Panel on Treatment of Pregnant Women with HIV Infection and Prevention of Perinatal Transmission. Available at http://aidsinfo.nih.gov/contentfiles/lvguidelines/PerinatalGL.pdf. Accessed Jan. 30 2018.

Pediatric AIDS Clinical Trials Group (PACTG) 076

	PACTG 076 (1994)
Design	Phase III, randomized, double-blind, placebo-controlled trial
Purpose	To evaluate ZDV in prevention of vertical transmission of HIV
Intervention	• Mother: ZDV 100 mg 5x daily during pregnancy + IV ZDV during labor • Infant: ZDV 2 mg/kg PO q6h x 6 weeks
Results	• 53/364 total evaluable infants had HIV infection • Placebo transmission: 25.5% • ZDV transmission: 8.3%
Limitations	• Women did not receive cART during pregnancy • ZDV side effect: Anemia (mild)
Conclusion	ZDV treatment reduces the risk of transmission of HIV

Source: Connor E, et al. N Engl J Med. 1994;331:1173-80.

PACTG 316

	PACTG 316 (2002)
Design	Phase III randomized, blinded, placebo-controlled study
Purpose	To evaluate 2-dose nevirapine (NVP) in reduction of perinatal HIV transmission
Intervention	• Mother: NVP 200 mg after onset of labor • Infant: NVP 2 mg/kg PO between 48 and 72 hours after birth
Results	Trial stopped early because overall transmission rate significantly lower than assumed for the study design • 1.4% nevirapine vs 1.6% placebo
Limitations	• PACTG 076 ZDV regimen received as minimum ARV therapy • 34% had cesarean delivery
Conclusion	No benefit from additional intrapartum/newborn NVP

Source: Dorenbaum A, et al. JAMA. 2002;288(2):189-98.

IV ZDV in cART Era

Briand N, et al (2013)	
Purpose	Evaluate impact of IV ZDV according to viral load and obstetrical conditions in prevention of mother-to-child transmission (MTCT)
Population	HIV-1 – infected women in the French Perinatal Cohort (Jan. 1997 and Dec. 2010) who received cART during pregnancy and did not breastfeed

Results	• IV ZDV used in 95.2% of 11,538 deliveries
	• Lack of IV ZDV associated with: older age (>35 years), multiparity, preterm and vaginal delivery, and high HIV RNA at delivery
	• **Women with viral load ≥ 1,000 copies/mL**
	  • Overall MTCT higher without IV ZDV (7.5% vs. 2.9%, p = 0.01)
	  • No difference in neonates with postnatal intensification therapy

Limitations	• Small proportion of HIV-infected women who did not receive IV ZDV • Few infected infants = not powered to detect risk in high-risk births • Observational study
Conclusions	IV ZDV reduces transmission in cases of virological failure; however, for women **with low viral loads at delivery**, in the absence of obstetrical risk factors, systematic IV ZDV appears to be unnecessary

Source: Briand N, et al. Clin Infect Dis. 2013;57(6):903-14.

Learning Assessment Q #2

Which of the following statements supports IV zidovudine as the intrapartum medication of choice?

A. ZDV reduces maternal HIV viral load

B. ZDV crosses the placenta readily

C. ZDV has a high cord-to-maternal blood ratio

D. ZDV penetrates the central nervous system

E. All of the above

Assessment Response #2

Which of the following statements supports IV zidovudine as the intrapartum medication of choice?

A. ZDV reduces maternal HIV viral load

B. ZDV crosses the placenta readily

C. ZDV has a high cord-to-maternal blood ratio

D. ZDV penetrates the central nervous system

E. All of the above

Infant ARV Prophylaxis

- All HIV-exposed infants should receive postpartum ARV drugs to reduce the risk of perinatal transmission of HIV
  - Initiated within 6 to 12 hours of delivery

- Combination infant prophylaxis regimen:
  - Mother did not receive antepartum or intrapartum ARV drugs
  - Mother received only intrapartum ARV drugs
  - Mother received antepartum ARV drugs without viral suppression
  - Mothers with acute or primary HIV infection during pregnancy or breastfeeding

- Premature infants: ZDV, lamivudine (3TC), and NVP are the only recommended ARV drugs

Source: Panel on Treatment of Pregnant Women with HIV Infection and Prevention of Perinatal Transmission. Available at http://aidsinfo.nih.gov/contentfiles/lvguidelines/PerinatalGL.pdf. Accessed Jan. 30 2018.

Overview of Newborn ARV Management

Category	Neonatal ARV Management
Low Risk of Perinatal HIV Transmission	4 weeks of ZDV
Higher Risk of Perinatal HIV Transmission	Combination ARV prophylaxis • 6 weeks of ZDV and 3 doses of NVP (prophylaxis dosage) • Empiric HIV therapy: ZDV + 3TC + NVP (treatment dosage)
Presumed Newborn HIV Exposure	(Same as above) *Discontinue immediately if supplemental testing confirmed that mother does not have HIV*
Newborn with Confirmed HIV	Three-drug combination ARV regimen at treatment dosage

Source: Panel on Treatment of Pregnant Women with HIV Infection and Prevention of Perinatal Transmission. Available at http://aidsinfo.nih.gov/contentfiles/lvguidelines/PerinatalGL.pdf. Accessed Jan. 30 2018.

Neonatal Dosing

	Dosing		Duration
ZDV	≥35 weeks	4 mg/kg PO BID	Birth through 4-6 weeks
	≥30 to <35 weeks	2 mg/kg PO BID x 2w then 3 mg/kg PO BID	
	<30 weeks	2 mg PO BID x 4w then 3 mg/kg PO BID	
3TC	≥32 weeks	2 mg/kg PO BID x 4w then 4 mg/kg PO BID	Birth through 2-6 weeks
NVP Prophylaxis	BW 1.5-2 kg	8 mg/**dose** PO	Within 48 hours of birth, 48 hours after 1st dose, 96 hours after 2nd dose
	BW > 2 kg	12 mg/**dose** PO	
NVP Treatment	≥37 weeks	6 mg/kg PO BID	Birth through 2-6 weeks
	34 to < 37 weeks	4 mg/kg PO BID x 1w then 6 mg/kg PO BID	

Source: Panel on Treatment of Pregnant Women with HIV Infection and Prevention of Perinatal Transmission. Available at http://aidsinfo.nih.gov/contentfiles/lvguidelines/PerinatalGL.pdf. Accessed Jan. 30 2018.

Infant ZDV Prophylaxis

- PACTG 076 and 316 studied six-week regimen
- European countries recommend four-week ZDV regimen for infants born to mothers with viral suppression
  - Reported to allow earlier recovery of anemia compared to six-week regimen in otherwise healthy infants
  - **Four-week neonatal ZDV regimen recommended** by the Panel if mother received standard ART during pregnancy with sustained viral suppression
- Six-week neonatal ZDV regimen recommended for all combination infant prophylaxis regimens

Source: Panel on Treatment of Pregnant Women with HIV Infection and Prevention of Perinatal Transmission. Available at http://aidsinfo.nih.gov/contentfiles/lvguidelines/PerinatalGL.pdf. Accessed Jan. 30 2018.

Nielsen-Saines, et al. (2012)

- The only randomized clinical trial of combination prophylaxis in infants at high risk of HIV acquisition
- Population: Newborns born to women with HIV who did not receive any ARV drugs during pregnancy
- Three neonatal regimens:

ZDV-alone group	ZDV x six weeks
Two-drug group	ZDV x six weeks PLUS NVP x 3 doses during the first eight days of life
Three-drug group	ZDV x six weeks PLUS nelfinavir + 3TC x two weeks

- Primary outcome: HIV-1 infection at three months in infants uninfected at birth

Source: Nielsen-Saines K, et al. N Engl J Med. 2012;366(25):2368-79.

Nielsen-Saines, et al. (2012)

	N = 1,684	Transmission rate = 8.5%
ZDV-alone group	566	11.0%
Two-drug group	562	7.1% (p=0.03)
Three-drug group	556	7.4% (p=0.03)

- Multivariate analysis of associations with transmission:
  - ZDV monotherapy
  - Higher maternal viral load
  - Maternal use of illegal substances

- Three-drug group had increased rate of neutropenia compared to ZDV alone (27.5% vs. 16.4%, p<0.0001)

- Conclusion: In neonates whose mothers did **not** receive ART during pregnancy, prophylaxis with two- **OR** three-drug ART regimens are both superior to ZDV alone

Source: Nielsen-Saines K, et al. N Engl J Med. 2012;366(25):2368-79.

The "Mississippi Baby" (2013)

- Woman with no prenatal care diagnosed with HIV-1 during vaginal delivery at 35 weeks' gestation (*HIV-1 RNA: 2,423 copies/mL*)
- Infant began ART 30 hours after birth until 18 months of age

HIV-1 RNA	Results	ART
31 hours	19,812 copies/mL	ZDV, 3TC, and NVP
6 days	2,617 copies/mL	ZDV, 3TC, and NVP
11 days	516 copies/mL	ZDV, 3TC, and lopinavir/ritonavir
19 days	265 copies/mL	ZDV, 3TC, and lopinavir/ritonavir
29 days	<48 copies/mL	ZDV, 3TC, and lopinavir/ritonavir

ZDV 2 mg/kg q6h, 3TC 4 mg/kg BID, NVP 2 mg/kg BID

- HIV-1 RNA and HIV-1 antibodies remained undetectable through 30 months of age → *case published*
- **Virologic rebound before the child turned four years of age**

Source: Persaud D, et al. N Engl J Med. 2013; 369;1828-35.

Three-Drug Prophylaxis

- Bitnun A, et al. (2014)
  - Infants born to HIV-infected mothers started on treatment doses of cART within 72 hours of birth at three Canadian centers
    - ZDV, 3TC, and NVP
  - 12/136 (8.8%) cART-treated infants vertically infected
    - 4 achieved sustained virologic suppression
    - cART NOT discontinued by time of publication
  - Limitations: No assessment of safety or efficacy relative to alternative drug regimens

- Conclusion: In perinatally HIV-1-infected newborns, initiation of cART within 72 hours of birth may significantly reduce the size of the HIV-1 reservoirs

Source: Bitnun A, et al. Clin Infect Dis, 2014;59(7):1012-9.

Three-Drug Prophylaxis

- Kakkar FW, et al. (2016)
  - Evaluation of safety and tolerability of triple cART for post-exposure prophylaxis for HIV-exposed neonates
    - Compared to ZDV-only group
    - Regimen prescribed at treatment doses

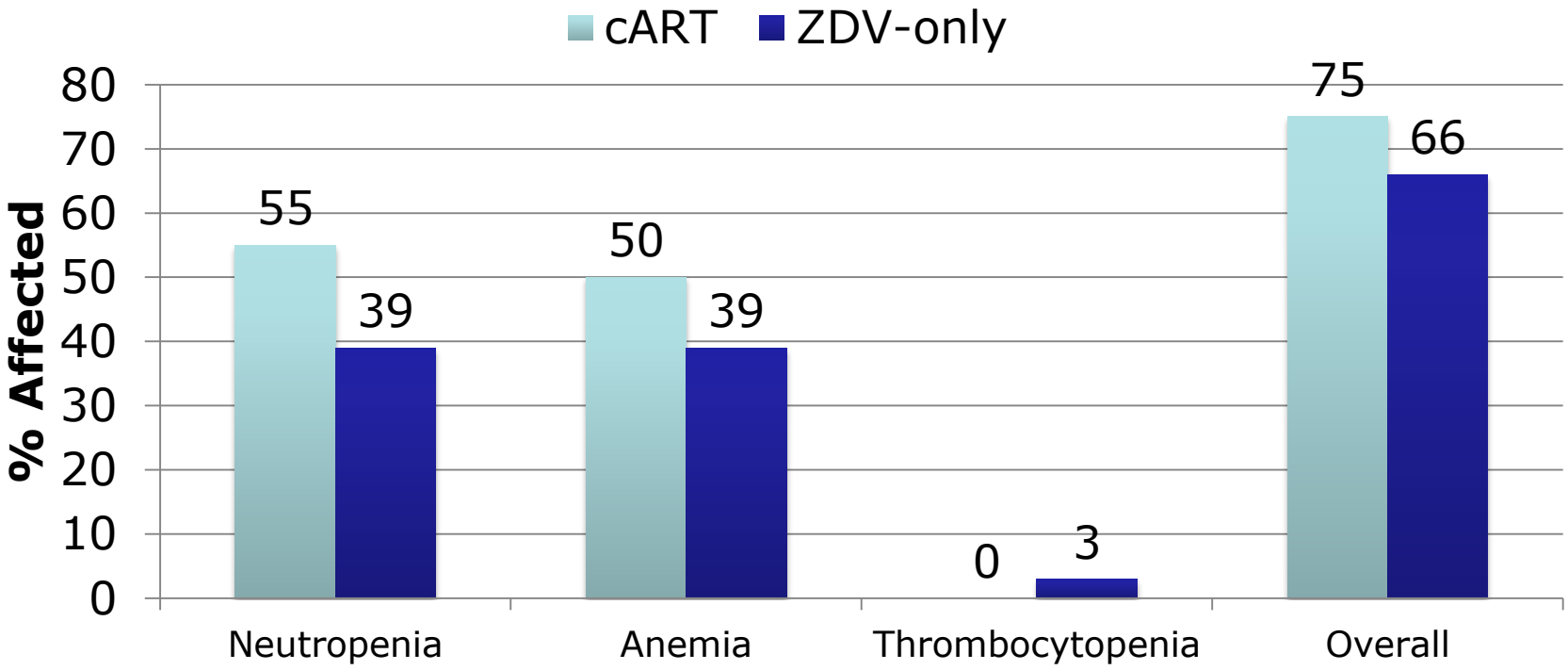
	cART (N = 148)	**ZDV only (N = 145)**	**P-value**
Non-specific signs and symptoms	10.2%	0%	<0.001
Premature discontinuation*	9.5%	2.1%	=0.01
Lower mean Hgb (decreased of 2.07 g/dL) over 6-month period compared with ZDV recipients			

*Anemia, neutropenia, nonspecific signs and symptoms, parental decision

Source: Kakkar FW, et al. J Int AIDS Soc. 2016; 19(1):20520.

Neonatal cART Adverse Events

- Smith C, et al. (2015): Retrospective review
  - cART (n = 36), ZDV-alone (n = 112)
  - No statistically significant differences



Source: Smith C,et al. PLoS ONE. 2015. 10(5):e0127062.

Three-Drug Controversy

Support

- Consistent with adult prophylaxis
- Retrospective studies demonstrate cART is "generally well-tolerated"

Concerns

- Limited NVP safety data at therapeutic doses
- Lopinavir/ritonavir not recommended for neonates < 14 days

Source: Panel on Treatment of Pregnant Women with HIV Infection and Prevention of Perinatal Transmission. Available at http://aidsinfo.nih.gov/contentfiles/lvguidelines/PerinatalGL.pdf. Accessed Jan. 30 2018.

Learning Assessment Q #3

TRUE or FALSE: Current literature supports the routine administration of a three-drug antiretroviral regimen as compared to a two-drug antiretroviral regimen for infant HIV prophylaxis.

A. TRUE

B. FALSE

Assessment Response #3

TRUE or FALSE: Current literature supports the routine administration of a three-drug antiretroviral regimen as compared to a two-drug antiretroviral regimen for infant HIV prophylaxis.

A. TRUE

B. FALSE

Panel Recommendations

- Combination ARV prophylaxis regimen recommended in infants at high risk of HIV acquisition

- "… the Panel was unable to reach clear consensus on the specific ARV prophylaxis regimen in these infants…"

- Specific agents
  - All infants should receive six weeks of ZDV
  - Optimal duration of 3TC and NVP is unknown
  - Dosing of NVP under investigation

Source: Panel on Treatment of Pregnant Women with HIV Infection and Prevention of Perinatal Transmission. Available at http://aidsinfo.nih.gov/contentfiles/lvguidelines/PerinatalGL.pdf. Accessed Jan. 30 2018.

Clinical Trials in Progress…

- International Maternal Pediatric and Adolescent AIDS Clinical Trials (IMPAACT) network
  - IMPAACT P1115: Very Early Intensive Treatment of HIV-Infected Infants to Achieve HIV Remission
  - IMPAACT P1097: Evaluating the Safety and Pharmacokinetics of Raltegravir in Infants

- Infants known to be infected:
  - BHP-074: Early HIV Treatment in Botswana
  - Leopard Study: Latency and Early Neonatal Provision of Antiretroviral Drugs

Initial Postnatal Management

- Baseline complete blood count and differential
- Infants receiving ZDV/3TC-containing regimens:
  - Hemoglobin counts remeasured at 4 weeks
  - Neutrophil counts remeasured at 4 weeks
- PCP prophylaxis at 4 to 6 weeks upon completion of ARV prophylaxis regimen unless presumptive exclusion
- Counsel mothers to avoid breastfeeding and premastication
- Infants should be tested for HIV infection at baseline and at 14- to 21-days, 1- to 2-months, and 4- to 6-months

Source: Panel on Treatment of Pregnant Women with HIV Infection and Prevention of Perinatal Transmission. Available at http://aidsinfo.nih.gov/contentfiles/lvguidelines/PerinatalGL.pdf. Accessed Jan. 30 2018.

Discharge Medications

- Lamivudine 7.5 mg (2 mg/kg/dose) PO q12h x 7 days
- Zidovudine 15 mg (4 mg/kg/dose) PO q12h x 7 days
- Nevirapine 22 mg (6 mg/kg/dose) PO q12h x 7 days

- Day of life 12: Results of HIV DNA/RNA PCR undetectable

- Plan to discontinue nevirapine and lamivudine and to complete six weeks total ZDV prophylactic therapy

Critique of Therapy

- Maternal cART should have been maximized during pregnancy
- Administration of IV ZDV and cesarean delivery appropriate
- Infant prophylaxis
  - Considered high-risk, and, therefore, cART was indicated
  - There is no clear consensus on cART regimen
    - Three-drug regimens expose infants to a greater risk of adverse effects than ZDV-only regimens
    - There is no clear benefit of a three-drug regimen as opposed to a two-drug regimen for high-risk infants

Learning Assessment Q #4

Which of the following is/are potential concerns associated with combination antiretroviral therapy for infant HIV prophylaxis?

A. Anemia

B. Neutropenia

C. Non-adherence

D. Both A & B

E. All of the above

Assessment Response #4

Which of the following is/are potential concerns associated with combination antiretroviral therapy for infant HIV prophylaxis?

A. Anemia

B. Neutropenia

C. Non-adherence

D. Both A & B

E. All of the above

NIOSH Hazardous Drugs

- Drugs may be considered hazardous because they exhibit potential toxicity in humans, animal models, or in vitro systems

- "Universal precautions" cannot cover all exposure types
  - Group 1: Antineoplastic drugs
  - Group 2: Non-antineoplastic drugs that meet one or more of the NIOSH criteria for a hazardous drug
  - Group 3: Drugs that pose a reproductive risk

- All hazardous drugs should be appropriately labeled and handled to minimize risk

Sources: Connor TH, et al. NIOSH [2016] Cincinnati, OH: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Institute for Occupational Safety and Health, DHHS (NIOSH) Publication Number 2016-161 (Supersedes 2014-138).

NIOSH Hazardous Drugs

Medication	NIOSH Category	Supplemental Information	Manufacturer's Safe-Handling Guidance
Zidovudine (liquid)	Group 2	IARC Group 2B; FDA Pregnancy Category C	Child-resistant cap
Nevirapine (liquid)	Group 2	FDA Pregnancy Category B; in laboratory studies, hepatocellular adenomas and carcinomas at doses lower than human dose	Child-resistant cap

- NIOSH administration recommendations for oral liquids:
  - Double chemotherapy gloves
  - Protective gown
  - Eye/face protection, if potential to spit up

Sources: Connor TH, et al. NIOSH [2016] Cincinnati, OH: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Institute for Occupational Safety and Health, DHHS (NIOSH) Publication Number 2016-161 (Supersedes 2014-138).
Retrovir [package insert]. Research Triangle Park, NC: GlaxoSmithKline; 2008.
Viramune [package insert]. Ridgefield, CT: Boehringer Ingelheim Pharmaceuticals, Inc; 2017.

Learning Assessment Q for Pharmacy Technicians

Which of the following is a NIOSH recommendation for handling zidovudine syrup, a "Group 2" oral liquid?

A. Double chemotherapy gloves
B. Protective gown
C. Eye/face protection, if potential to spit up
D. All of the above

Assessment Response – Pharmacy Technicians

Which of the following is a NIOSH recommendation for handling zidovudine syrup, a "Group 2" oral liquid?

A. Double chemotherapy gloves
B. Protective gown
C. Eye/face protection if potential to spit up
D. All of the above

Summary

- There have been many developments in the prevention of transmission of HIV infection from mother to infant

- The optimal prophylactic cART regimen for high-risk infants is unknown, and further research is necessary in order to determine:
  - Selection of agents
  - Dosing of medications
  - Duration of therapy

- There exists insufficient data to support standard use of a three-drug prophylactic regimen for all high-risk infants