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INVESTOR UPDATE

OCTOBER 17, 2018

Forward-Looking Statements

These slides and the accompanying oral presentation contain forward-looking statements and information within the meaning of the Private Securities Litigation Reform Act of 1995 that are subject to risks, uncertainties and other factors, including the possibility that there may not be a viable continued development path for brincidofovir, that any clinical trials we may conduct will not demonstrate adequate efficacy and safety of brincidofovir, that the FDA and other regulatory authorities may not approve brincidofovir or brincidofovir-based regimens, and that marketing approvals, if granted, may have significant limitations on their use. As a result, brincidofovir may never be successfully commercialized. In addition, Chimerix may be unable to file for regulatory approval for brincidofovir with other regulatory authorities. Similar risks and uncertainties apply to our development of CMX521. These risks, uncertainties and other factors could cause actual results to differ materially from those referred to in the forward-looking statements. The reader is cautioned not to rely on these forward-looking statements. These and other risks are described in detail in Chimerix's Quarterly Report on Form 10-Q for the quarter ended June 30, 2018 and other documents subsequently filed with or furnished to the U.S. Securities and Exchange Commission. All forward-looking statements are based on information currently available to Chimerix, and Chimerix assumes no obligation to update any such forward-looking statements.

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Chimerix Investor Update: October 17, 2018

- M. Michelle Berrey, MD, MPH, President & CEO
  - Welcome and program overview
- Roy F. Chemaly, MD, MPH, Professor, Department of Infectious Diseases, University of Texas MD Anderson Cancer Center, Houston, TX
  - Why do we need a broad-spectrum antiviral?
- Garrett Nichols, MD, MS, Chief Medical Officer
  - AdAPT, AdVance, and BCV's utility in adenovirus beyond transplant
  - IV BCV for BK and HHV6
- Kevin Reeves, VP of Commercial
  - Growing market opportunities for oral and IV BCV
- Randall Lanier, PhD, Chief Science Officer
  - Norovirus clinical study update

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M. MICHELLE BERREY, MD, MPH
CORPORATE UPDATE

OCTOBER 17, 2018

Why Do We Believe in BCV?

- Over 1500 patients have been treated with brinci for life-threatening adenovirus infection
- High number of requests for BCV via EIND process
- BCV has been requested and administered for viral infections caused by nearly all dsDNA viruses
- Many transplant and ID physicians currently consider BCV their treatment of choice for adenovirus in transplant recipients and other patients
- We worked closely with European regulators to design a small, prospectively randomized study that gives us the opportunity to have short-course oral BCV reflected in our first indication
- …and now we are increasingly optimistic that AdV $AAUC_{0\text{-}16}$ could be accepted as a relevant surrogate marker for AdAPT, providing a path to accelerated approval

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Physicians Continue to Request BCV for Many Diseases

Adenovirus

Smallpox/Vaccinia

BKV: Hemorrhagic Cystitis

BKV: BKVAN (Kidney Tx)

HHV6: Encephalitis

CMV: Enteritis

CMV: Encephalitis

HSV Encephalitis

DRESS Syndrome

HPV: Recurrent Respiratory Papillomatosis (RRP)

Glioblastoma

CMV Encephalitis

HPV+ Head-and-Neck CA

HHV6: Alzheimer's Dz

Viral Myocarditis

JCV: PML (Progressive multifocal leukoencephalopathy)

Cowpox/Monkeypox

EBV: Burkitt's Lymphoma

Viral Encephalitis

MCV: Merkel Cell Virus

EBV: Post-transplant Lymphoproliferative Disease (PTLD)

Radiation sensitizer (option for renal insuff. pts)

Parvovirus

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BCV Has Been Used to Treat Multiple dsDNA Viral Infections

Viral Family	Virus	BCV	Clinical Efficacy Demonstrated in
Adenovirus	Adenovirus (AdV)	0.02	1500+ patients w AdV have received BCV
Polyoma	BK Virus (BKV)	0.13	New data in animal model confirms BCV activity (to be presented at Kidney Week), Ph 2 dose-ranging in planning
	JC Virus (JCV)	0.045	Oral BCV has been used in ~36 pts with PML or JC viremia IV BCV achieves higher CNS penetration
Papilloma	Human Papillomavirus (HPV)	17	BCV used in patients in expanded access trials
Herpes Viruses	Herpes Simplex Virus 1	0.01	BCV cleared acyclovir-resistant HSV-1 after HCT[1]
	Herpes Simplex Virus 2	0.02	BCV cleared acyclovir-resistant HSV-2 after HCT[2]
	Varicella Zoster Virus (VZV, HHV3)	0.0004	BCV demonstrated to prevent shingles post HCT[3]
	Epstein-Barr Virus (EBV, HHV4)	0.03	Anecdotal use in post-HCT viremia and disease
	Cytomegalovirus (CMV, HHV5)	0.001	Antiviral activity demonstrated in Ph 2[4] and Ph 3[5] trials
	Human Herpesvirus 6	0.003	Prevention of viremia and disease in subset analysis of Ph 3 HCT
	Human Herpesvirus 8	0.02	
Pox	Variola	0.1	Ongoing pivotal animal studies in collaboration with BARDA
	Vaccinia	0.8	Disseminated vaccinia cleared with BCV treatment[6]

1. Voight S et al. Transpl Infect Dis 2016;18:791–794
2. El-Haddad D et al. Antiviral Res. 2016;134:58-62.
3. Lee YJ et al. Transpl Infect Dis. 2018 Aug 18:e12977. doi: 10.1111/tid.12977. [Epub ahead of print]
5. Marty FM et al. Biol Blood Marrow Transplant 2016;22(3):S23.
6. Lederman E et al. J Infect Dis. 2012;206:1372-85.

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AdAPT: Positive Data Could Support Approval in the US

AdV $AAUC_{0\text{-}16}$	Survival	MAA	NDA
BCV superior	Numeric advantage	File	Accelerated Approval
BCV superior	Statistical advantage	File	Submit for full approval

- **If AdAPT shows BCV results in >1 log difference in AdV $AAUC_{0\text{-}16}$, based on the data from AdVance, there is an increased likelihood of improved overall survival**
  - FDA, under Commissioner Gottlieb, is looking to accelerate approvals of life-saving medicines, including new opportunities for sponsors to request Type C meetings in order to discuss surrogate markers
  - **Type C Meetings provide us with an opportunity to review AdVance and other independent data sets for the required Briefing Package – a compilation of all relevant materials that support the consideration of a new surrogate marker**

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Development and Procurement of BCV for Smallpox

- **Development of oral BCV** in two animal models is progressing in two final studies:
  1. **Rabbitpox** virus model: Adjunct pivotal cohort study now underway. Data expected in early 2019. Prior pivotal study demonstrated 100% survival in animals that received immediate treatment with brincidofovir.
  2. **Mouse pox** / ectromelia replicates respiratory infection route of human smallpox infection. We anticipate pivotal mouse pox study will be completed in 2019.

- **FY19 Funding** of $611M is now approved for BARDA together with PAHPA reauthorization
  - Multi-year funding for PAHPA (Pandemic All-Hazards Preparedness Act) has passed the House and is headed to Senate
    - **$7.1B** for Special Reserve Fund for FY2020-2028
  - With animal data in-hand in 2019, clarity on a procurement contract could occur

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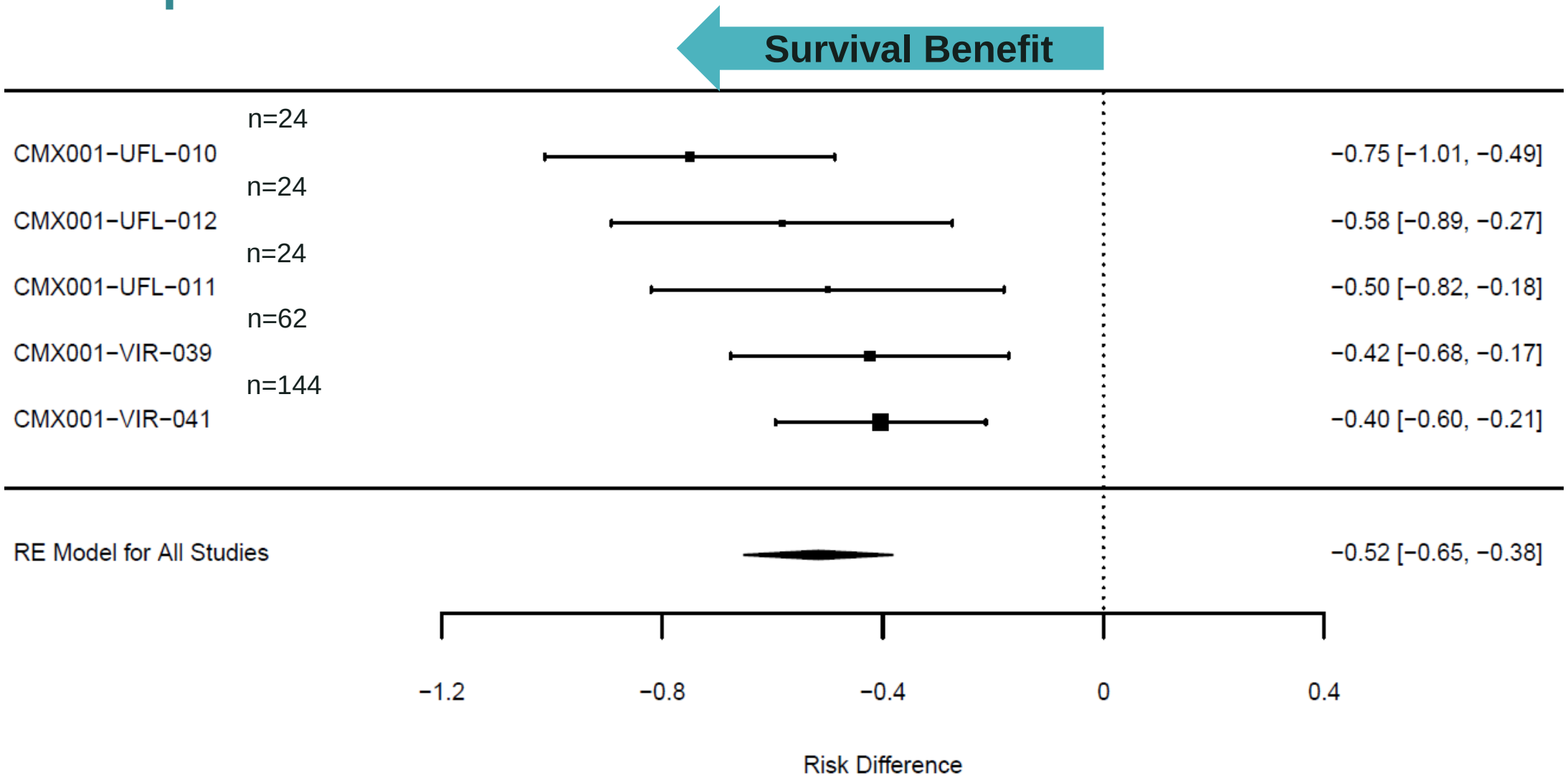
Brincidofovir has Demonstrated Survival Benefit in Multiple Rabbitpox Studies



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Oct 9th Blue Ribbon Study Panel on Biodefense Preparedness

- *"Most threats we face are global in nature. They're emerging diseases in far-away places. They are nation-state actors. And we have this* ***new phenomenon of manipulation of synthetic biology*** *that can pop up virtually anywhere. Intermittent or one-year federal funding for biodefense won't do the trick… five- or 10-year programs are going to be needed."* **Dr. Scott Lillibridge**, the US's first bioterrorism preparedness director at CDC in 1999. *(emphasis added)*

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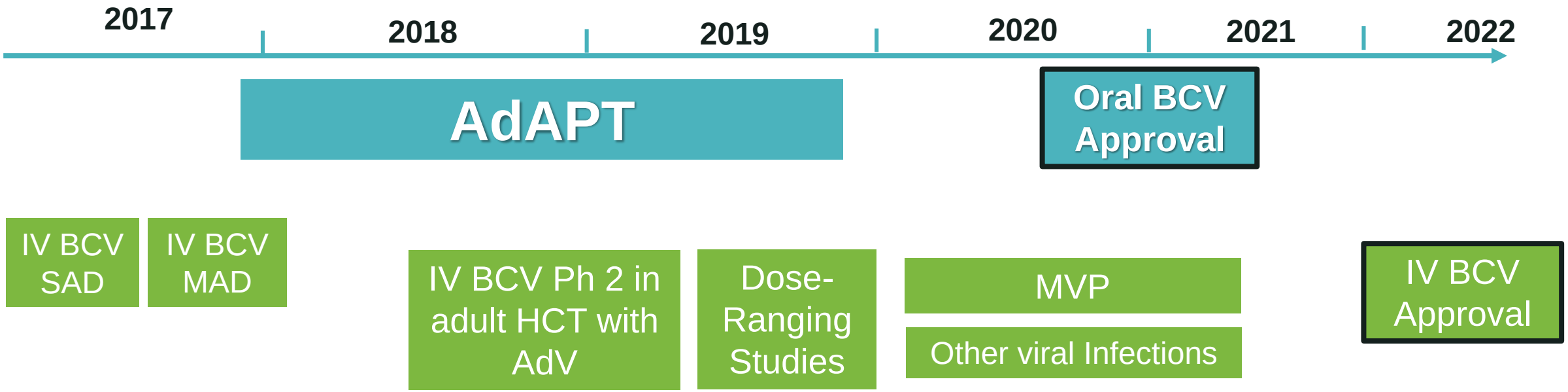
Anticipated Brincidofovir Milestones and Regulatory Decisions



- Oral short-course BCV for AdV in AdAPT expected to be enrolled in 2019
- Open-label Ph 2 IV BCV studies in adult patients expected to provide data in late 2018/early 2019
- IV BCV dose-ranging expected to be conducted in other serious viral infections: BKV & HHV-6
- IV BCV may allow longer duration dosing for prevention of multi-viral infection

All timelines are estimated

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CMRX: Developing Solutions for Immunocompromised Patients

- Experienced and committed management team with proven track records developing first-in-class antivirals and first-in-indication commercial launches
- Proprietary lipid-conjugate technology and large chemical library has led to two unpartnered and one partnered clinical-stage compounds
  - Brincidofovir (CMX001, BCV): first broad-spectrum antiviral in development
  - CMX521: investigational nucleoside for norovirus
  - CMX157: licensed to ContraVir for hepatitis B
- Well-capitalized to achieve planned milestones with $196M at the end of 2Q 2018
- Patent protection into 2034 for brincidofovir and 2036 for CMX521

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VIRAL INFECTIONS IN IMMUNOCOMPROMISED PATIENTS: WHY DO WE NEED A BROAD-SPECTRUM ANTIVIRAL?

Roy F. Chemaly, MD, MPH, FACP, FIDSA
Professor of Medicine
Director, Infection Control
Director, Clinical Virology Research Program
Department of Infectious Diseases, Infection Control and Employee Health

THE UNIVERSITY OF TEXAS
MD Anderson Cancer Center
Making Cancer History®

Disclosures

- Research grants paid to my institution:
  - Chimerix, Merck, Novartis, Shire, Aicuris, Oxford Immunotec
- Consultancy / speaker fee:
  - Chimerix, Merck, Shire, Oxford Immunotec, Astellas

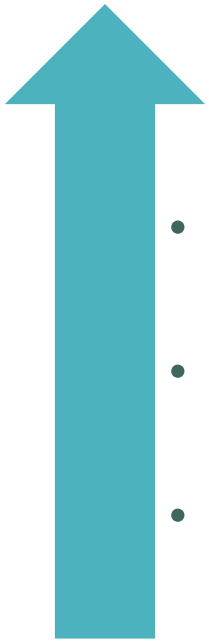
Why Do We Need a Broad-Spectrum Antiviral?

- A recipient of a hematopoeitic cell transplant (HCT) faces a 1-in-5 risk of mortality from infection in the first year after transplant[1]
  - High-risk HCT is the most rapidly growing segment of transplant
  - These patients receive more intense immunosuppression (ex vivo TCD, ATG, alemtuzumab, post transplant cyclophosphamide to prevent GVHD)
  - >90% of allo-HCT recipients reactivate 1 or more viruses
- In addition to transplant recipients, there is a growing population of patients at risk of viral diseases – patients on biologics, CAR T cell, or lifetime anticancer therapies
  - Ex: JC virus and PML reported in patients on long-term biologics
- The increasing association of viruses and some cancers may provide an opportunity for intervention at an earlier stage of disease

[1] CIBMTR.org

Hematopoietic Stem Cell Transplantation (HCT): A Primer

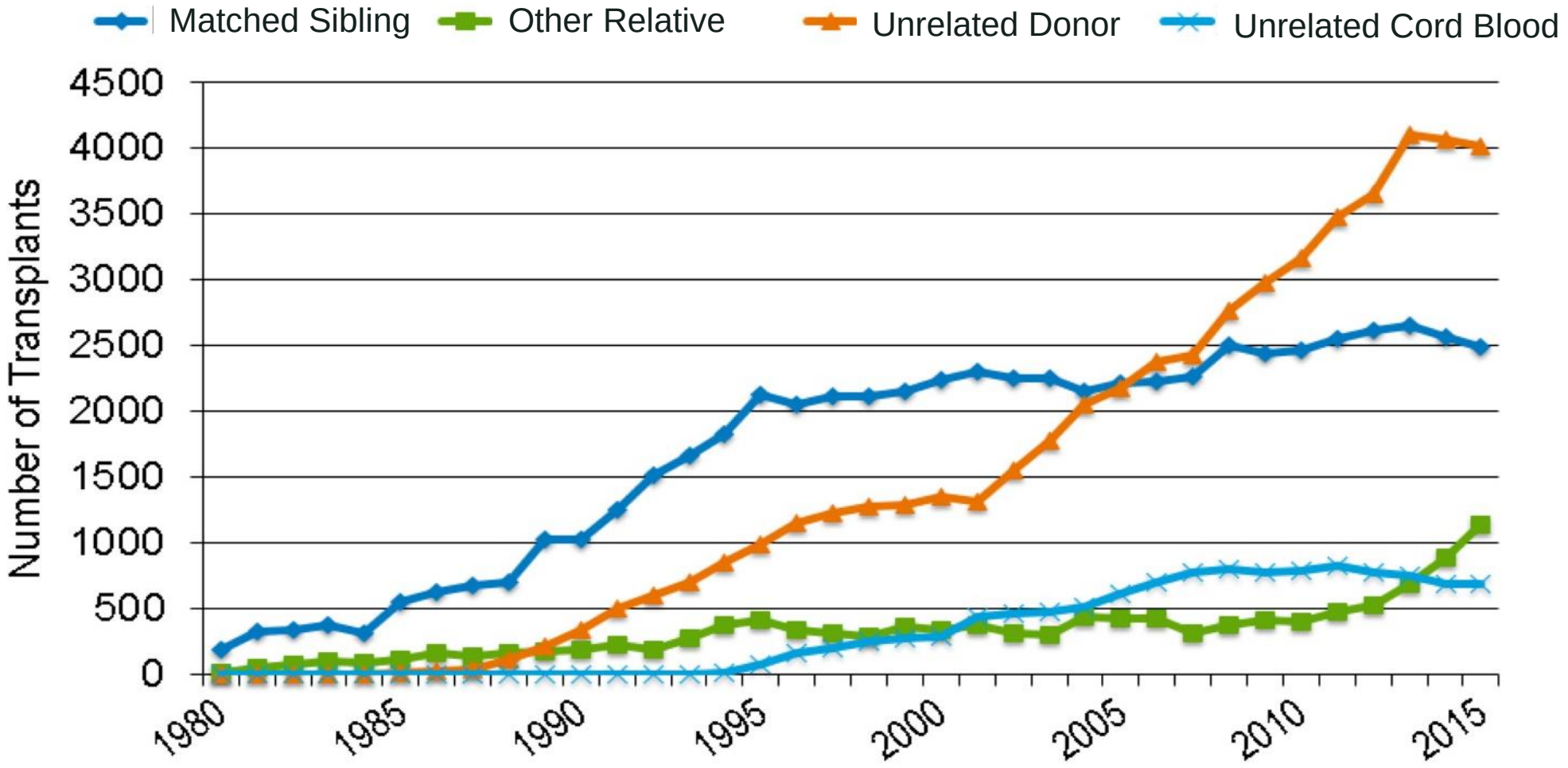
- Allogeneic HCT (allo-HCT): infusion of donor stem cells
  - Unrelated cord blood HCT (donor is immune naïve infant)
  - Haploidentical HCT (donor is a parent – half genetic match)
  - Mismatched unrelated donor HCT (moderate genetic match)
  - Matched unrelated donor HCT (high genetic match)
  - Matched related sibling allo-HCT (highest genetic match)



- **Increasing risk of GVHD**
- **Increasing immunosuppression**
- **Increasing risk for viral infections**

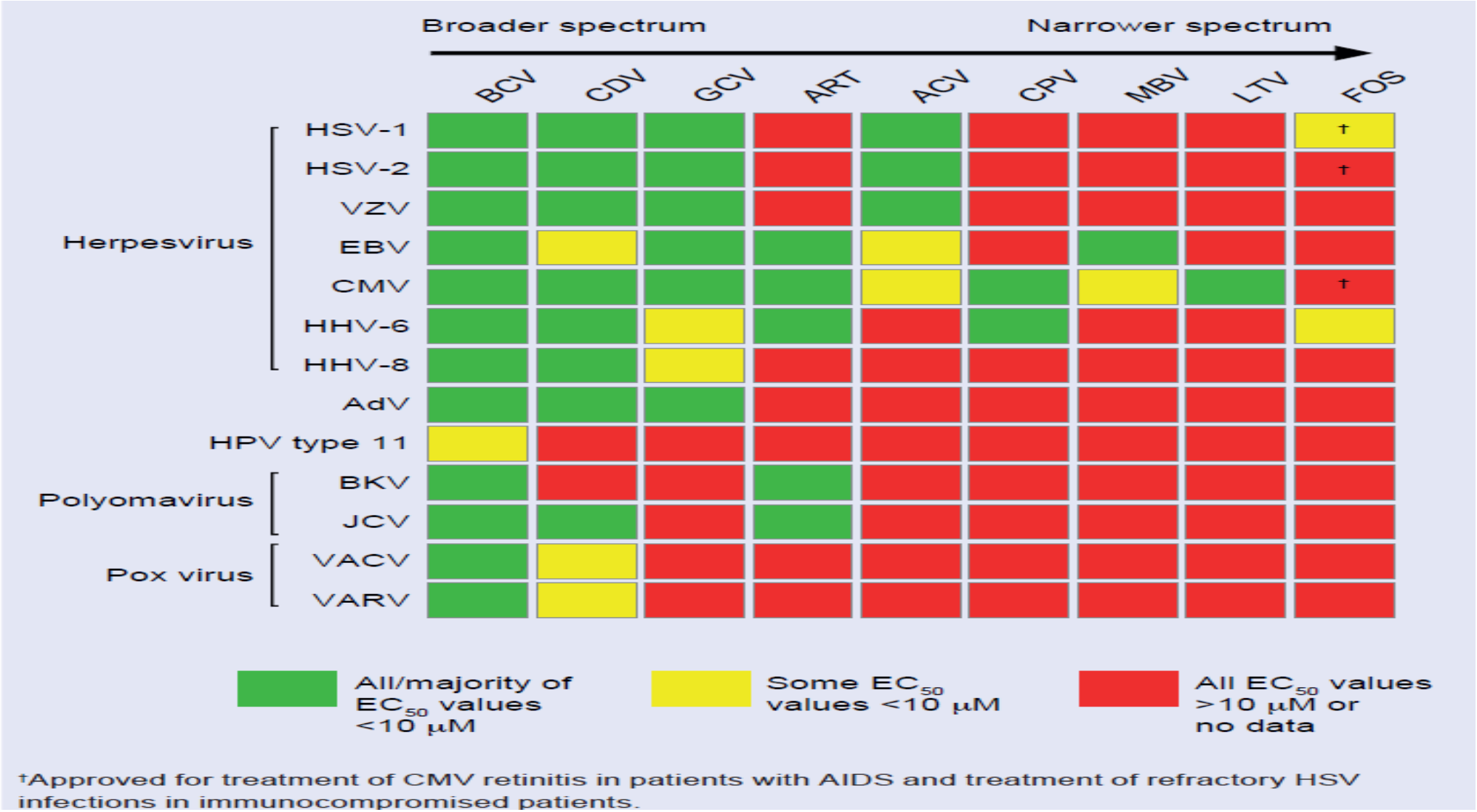
- Autologous HCT (auto-HCT): infusion of patient's own stem cells

Increasing Rate of High Risk Allo-HCT is Driving Growth



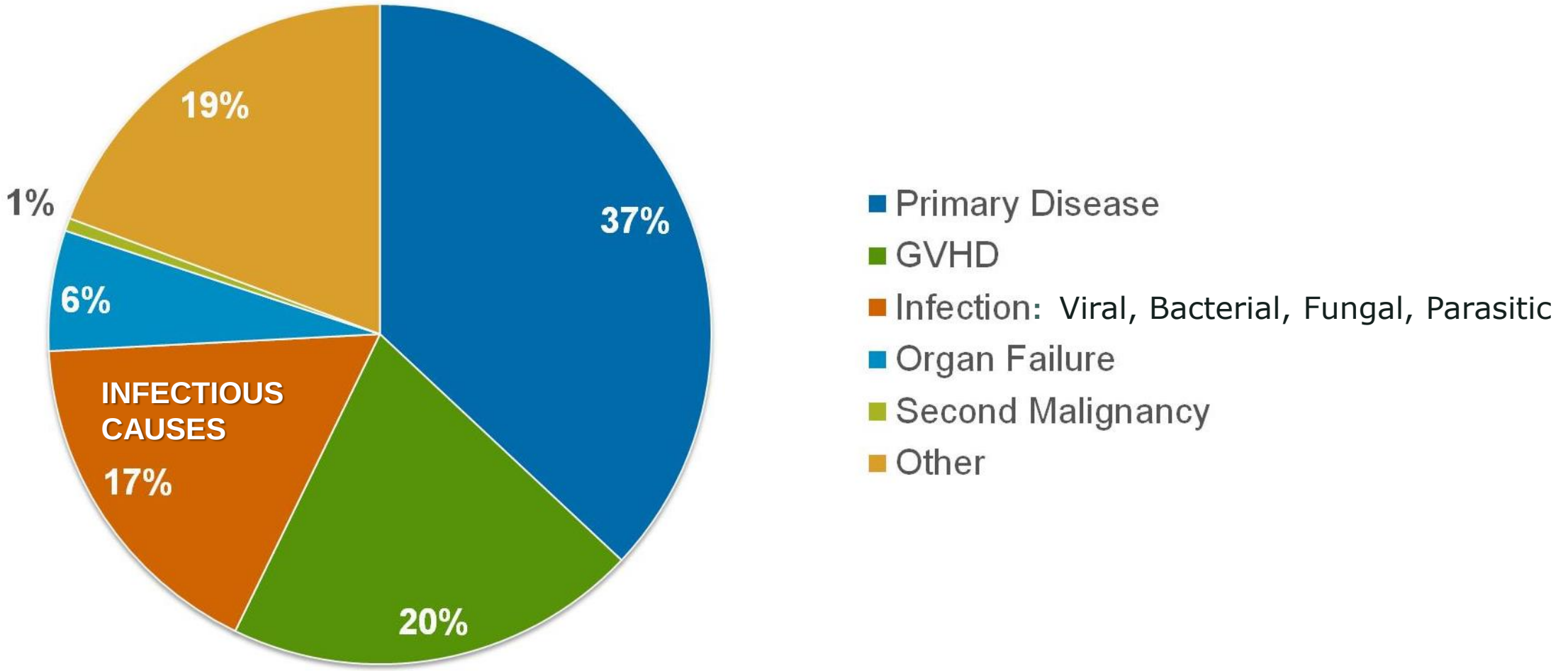
Source: CIBMTR

BCV: Broad Spectrum and High Potency vs. Other Antivirals
Results from a systematic literature review



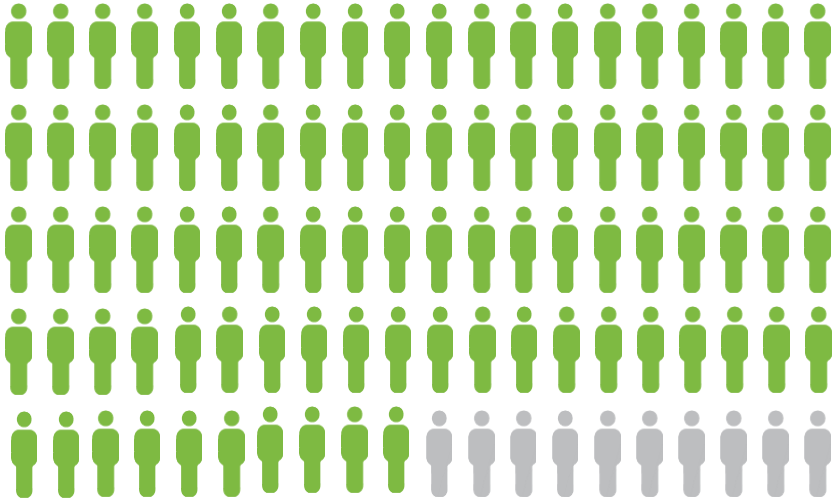
Chemaly RF et al. Presented at ESCV 2018, Athens, Greece

Infections and GVHD are the Most Frequent Causes of Non-Relapse Mortality After Bone Marrow Transplantation



Source: CIBMTR

A Majority of HCT recipients Have 2 or More Viral Infections



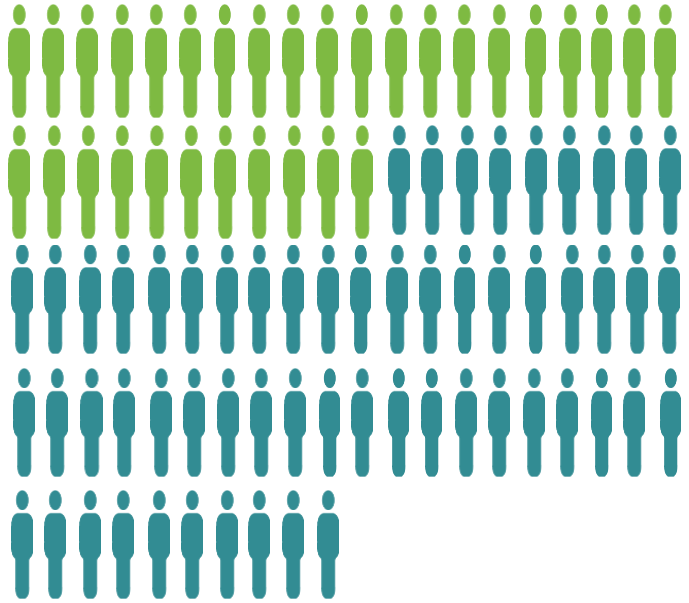
At least one DNA Virus in 363/404=

90%

2/3 have two or more DNA viruses

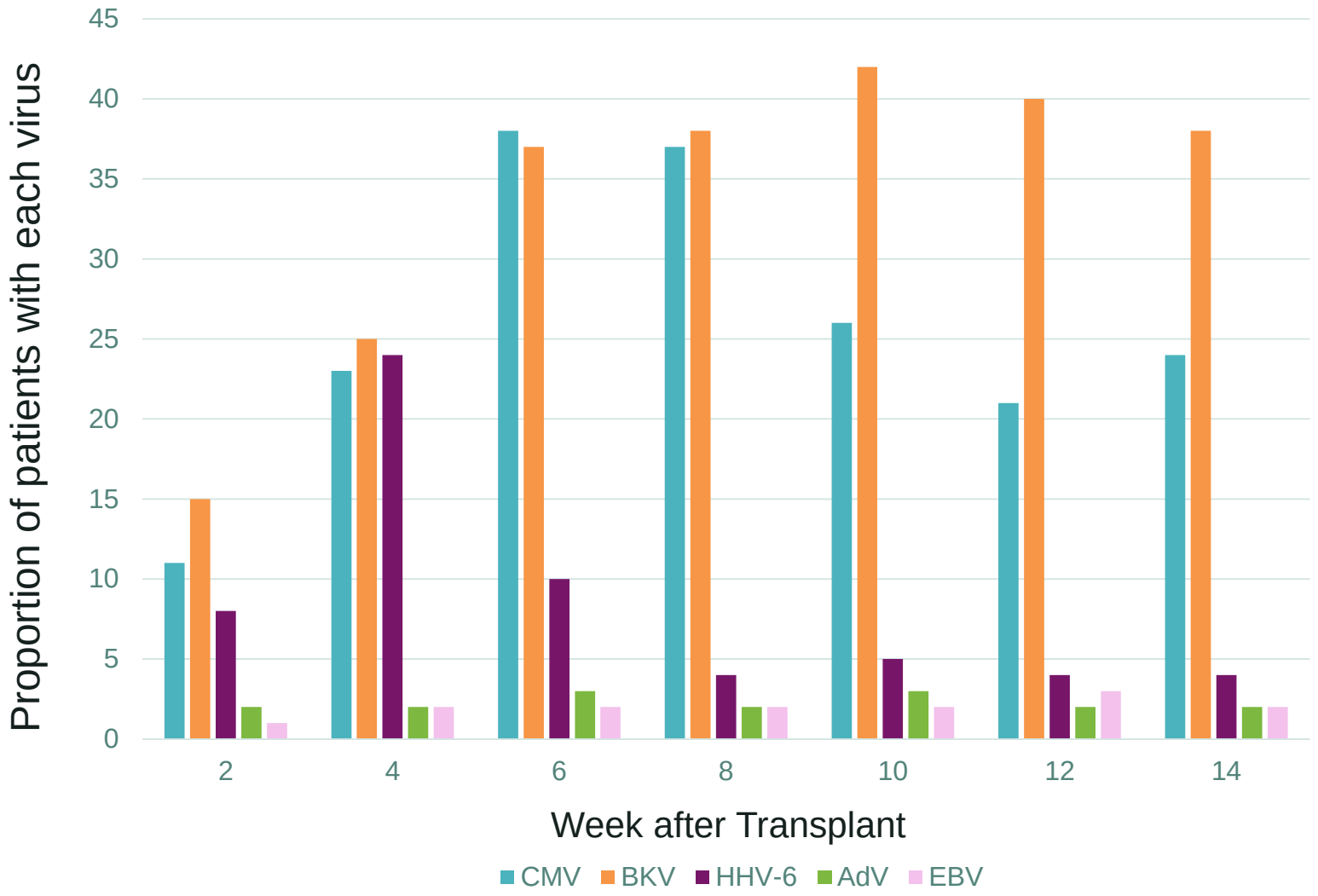
66%

1 in 3 HCT recipients had ≥3 DNA viral infections detected



Hill JA et al. Blood. 2017 Feb 16.

Multiple Viral Infections Reactivate and Persist After HCT



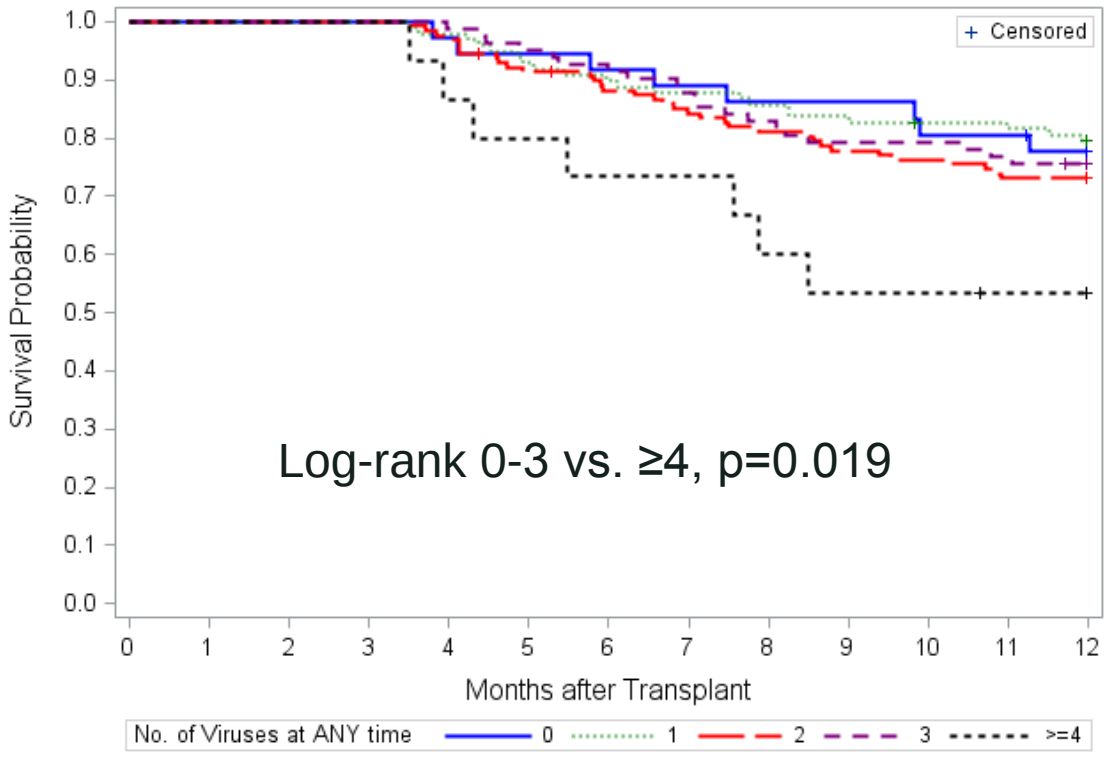
Cumulative Incidence First 100 Days:

CMV	64%
BKV	54%
HHV-6	47%
AdV	10%
EBV	9%

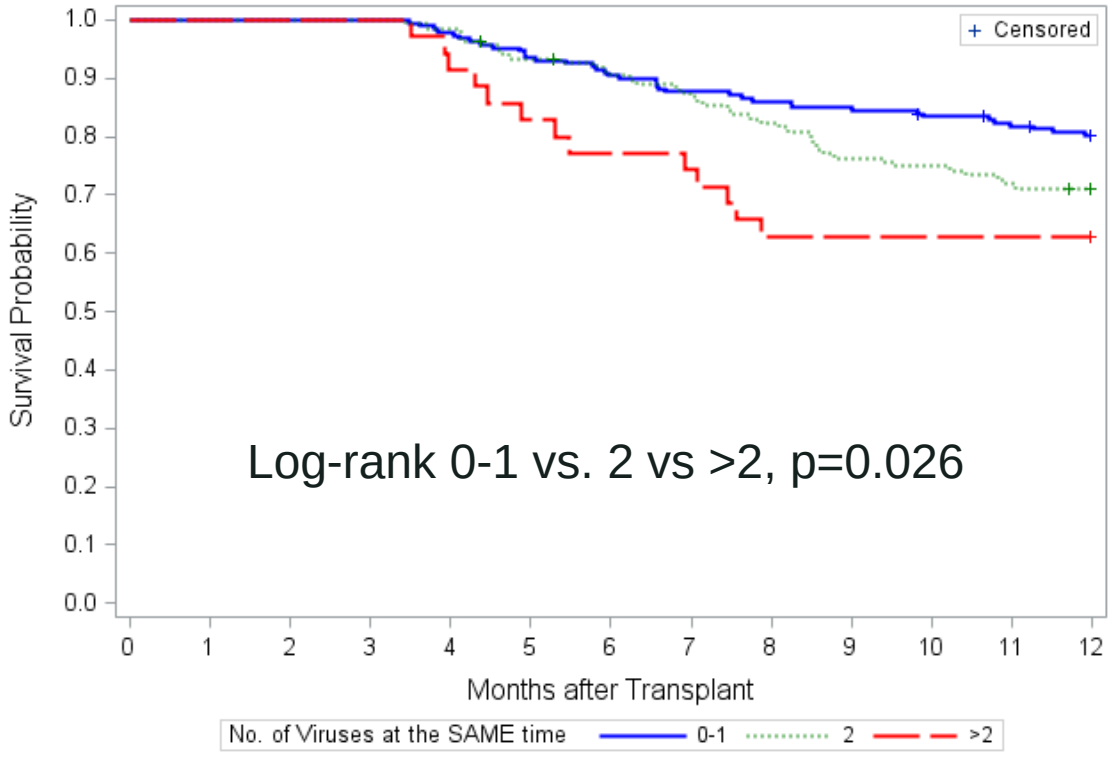
Hill JA et al. Blood. 2017 Feb 16.

More DNA Viruses Reactivating = Higher Mortality

Number of DNA viruses at any time



Number of DNA viruses at the same time



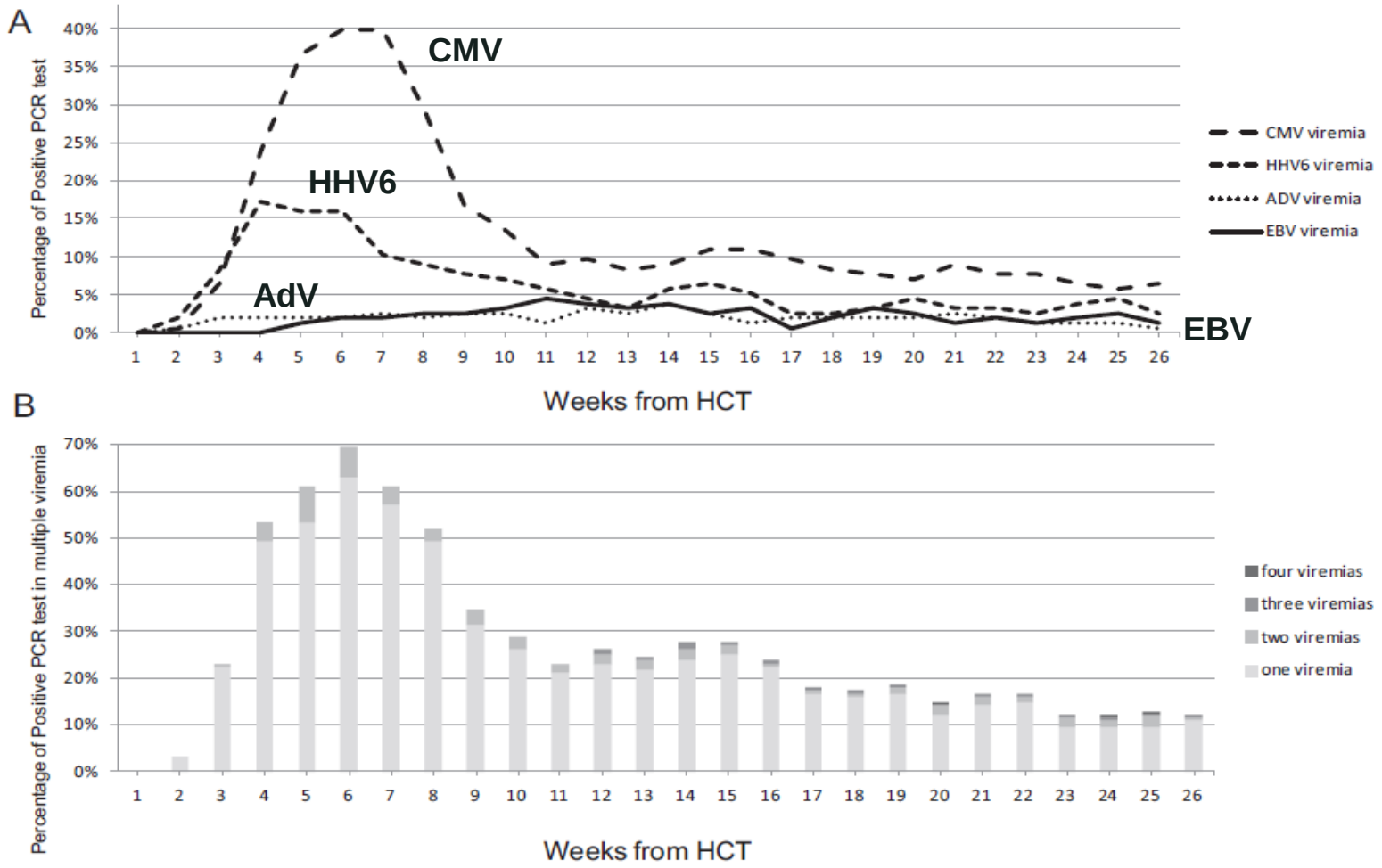
Cumulative viral load AUC was associated with mortality, after adjusting for immune reconstitution

Hill et al, Blood 2017

Multi-Viral Infections Are Common after T-cell Depletion

Yao-Ting Huang [1], Seong Jin Kim [1], Yeon Joo Lee [1,2], Daniel Burack [1], Paige Nichols [1], Molly Maloy [3], Miguel-Angel Perales [2,3], Sergio A. Giralt [2,3], Ann A. Jakubowski [2,3], Genovefa A. Papanicolaou [1,2,*]

Biol Blood Marrow Transplant 23 (2017) 1759–1766



Management of Multi-Viral Infections After HCT: Prophylaxis vs. Pre-emptive Treatment

Antiviral drugs	Target	Prophylaxis
▪ Ganciclovir/VGCV	Herpesviruses	Effective but toxic (myelotoxicity)
▪ Foscarnet	Herpesviruses	No proven prophylaxis efficacy Renal Toxicity
▪ Brincidofovir	Herpesviruses, ADV, BKV, HPV	Oral BCV under study as preemptive therapy for AdV to decrease GI AEs; IV BCV in Ph 2
Cellular therapy		
▪ Virus-specific T cells	CMV, EBV, ADV, BKV	No controlled data
▪ NK cells		

BK VIRUS

BK Virus: Unmet Need in HCT and Kidney Transplant

BKV Hemorrhagic Cystitis (HC)

- Clinical symptoms/signs of cystitis, such as dysuria, abdominal pain
- Hematuria Grade ≥2
- BK Virus in urine > 7 $\log_{10}$ copies /mL

BKV viremia of >3–4 $\log_{10}$ copies/mL frequently reported during HC

BKV Nephritis

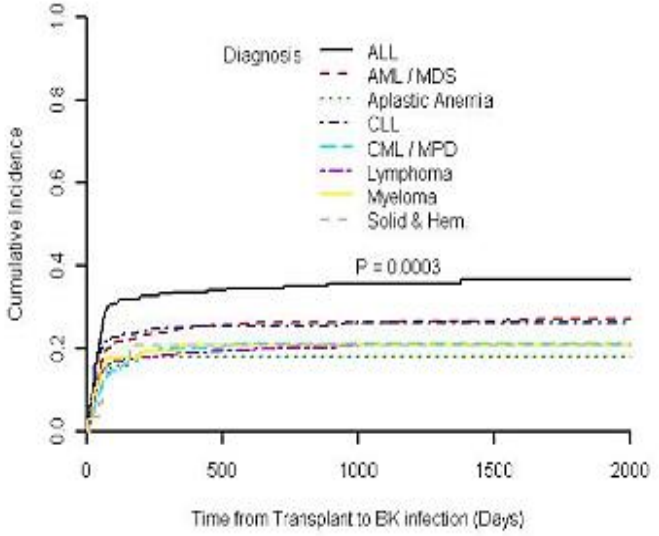
- BK viremia > 6 $\log_{10}$ copies /mL
- Biopsy showing positive SV40 staining
- Cytopathic changes of tubular epithelial cells

Cesaro S et al. J Antimicrob Chemother 2018:73:12

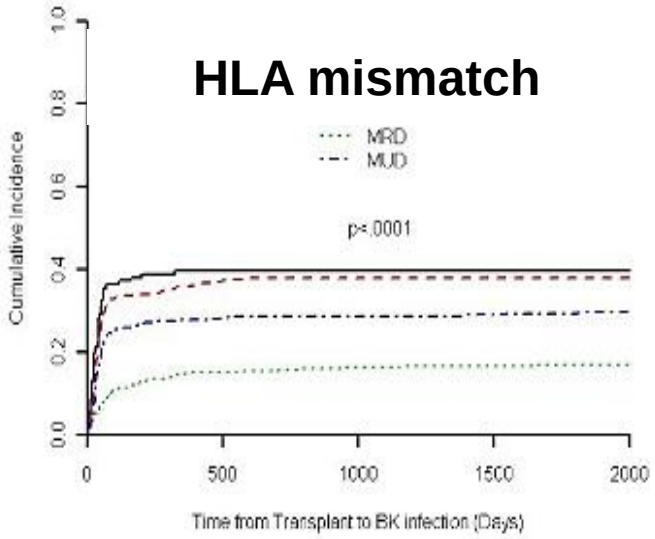
BKV HC Occurs in 10-25% of HCT

Setting	Cumulative incidence, median (range)	No. of patients
Allo-HSCT	13% (7–25)	2096
Haplo-HCT with post-transplant cyclophosphamide exposure	24.5% (19–54)	179
Auto-HCT	0	118
Adults	16% (7–54)	1413
Children	18% (8–25)	724
Adult and pediatric population	16% (13–19)	206

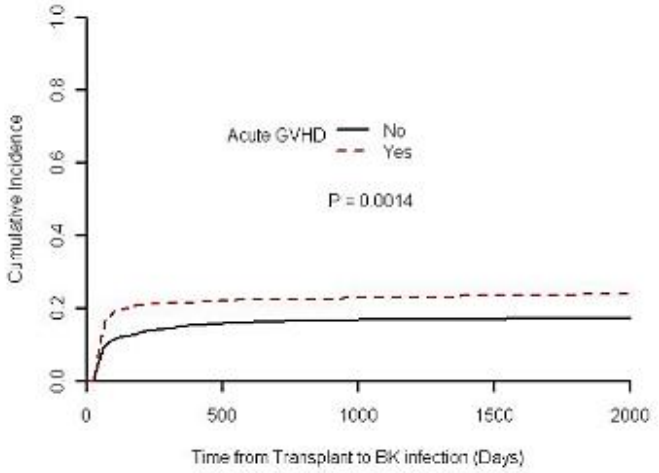
Cesaro S et al. J Antimicrob Chemother 2018:73:12



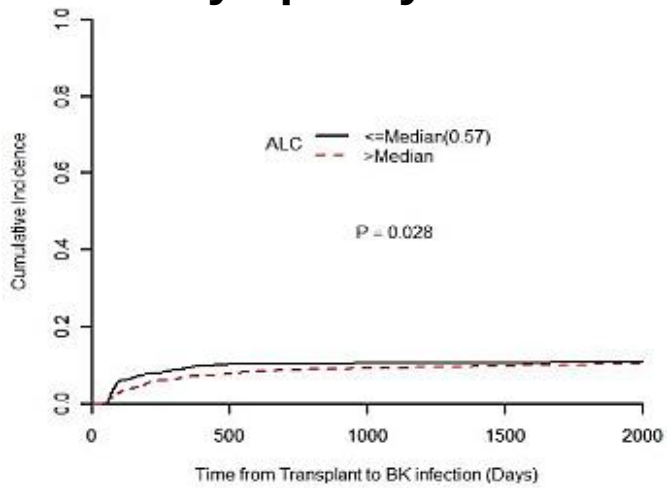
HLA mismatch



aGVHD



Lymphocyte count

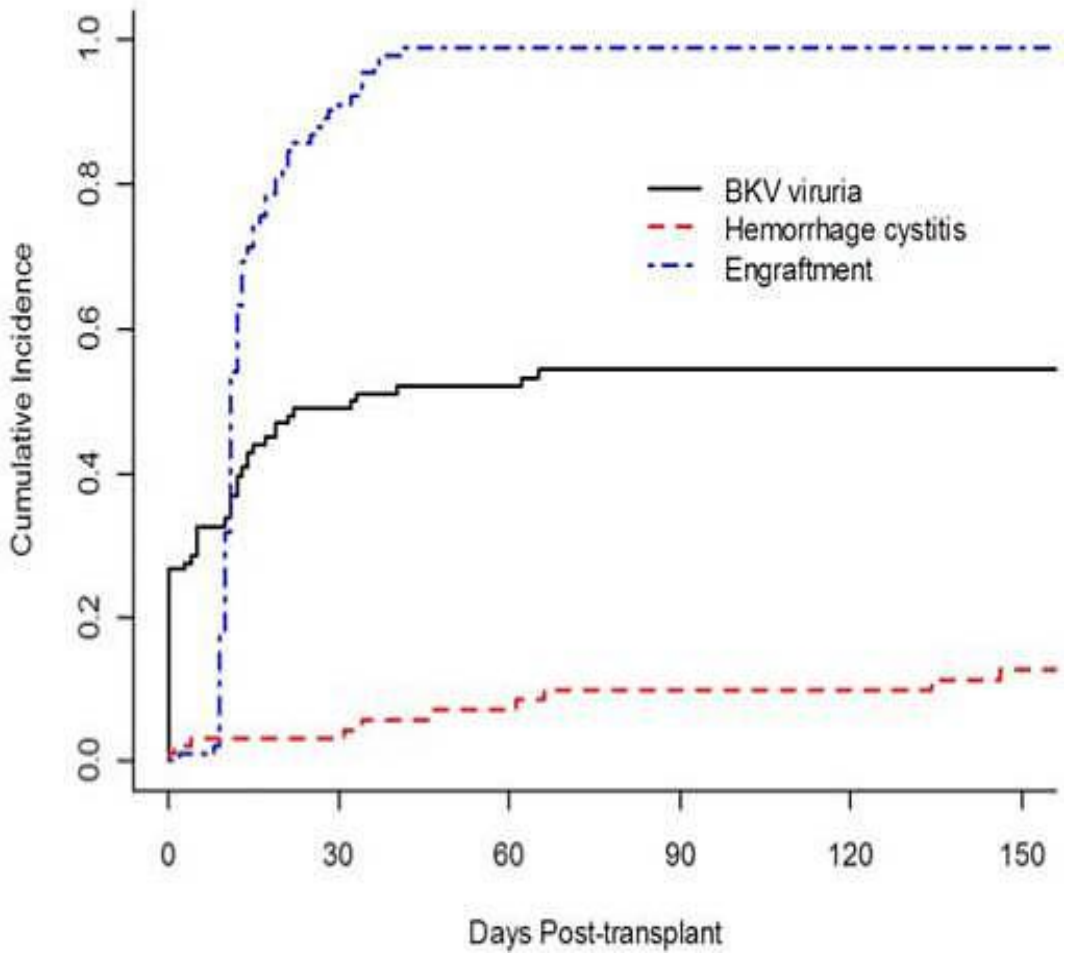


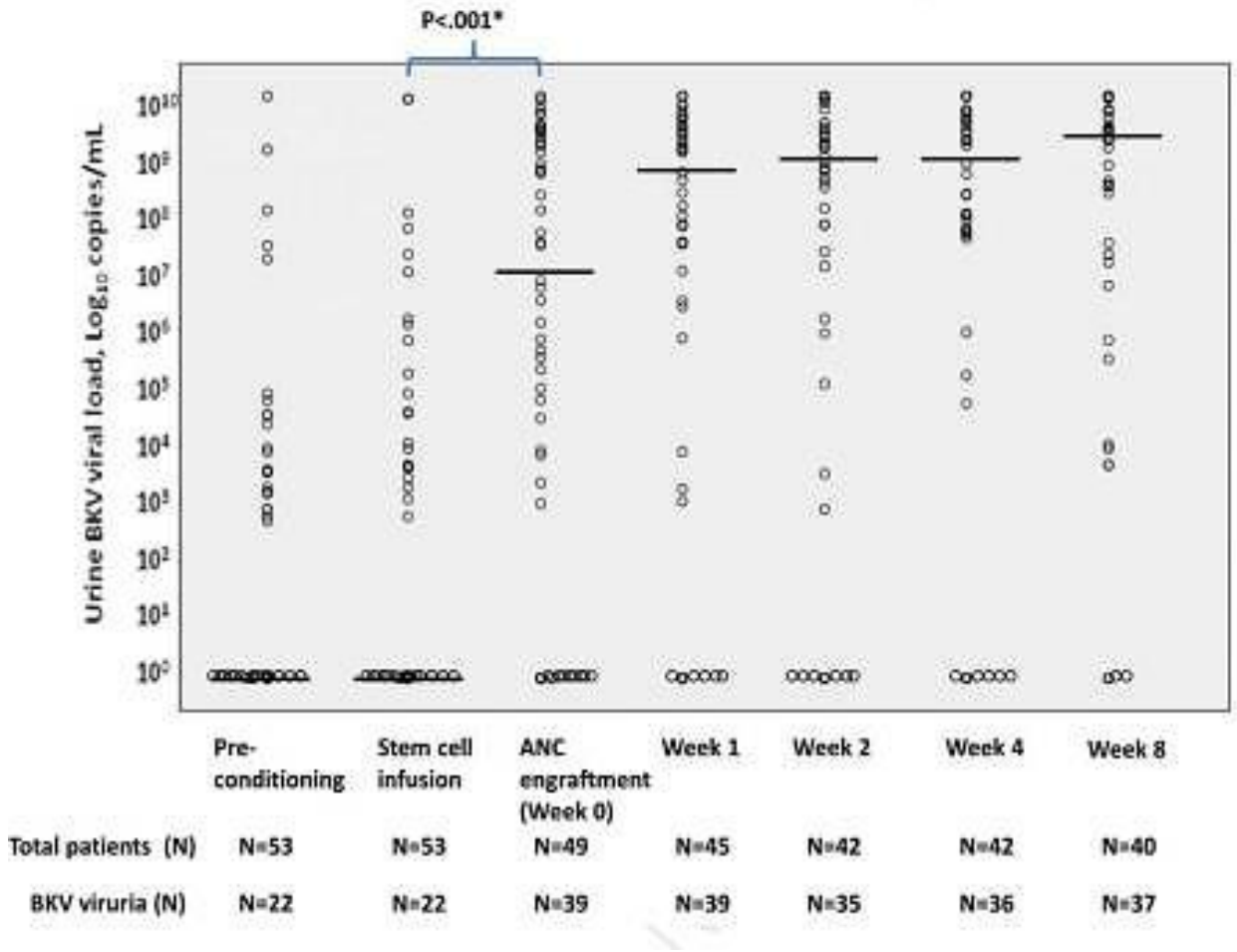
Risk Factors for BK infection

- Myeloablative conditioning (busulfan)
- Cord blood transplant
- CMV infection
- High BKV antibody Pre HCT

Abudayyeh A Transpl Infect Dis. 2017;19;
Rorije NMG Biol Blood Marrow transplant 2014;20:564

BKV Viruria Is Common and Persistent after HCT

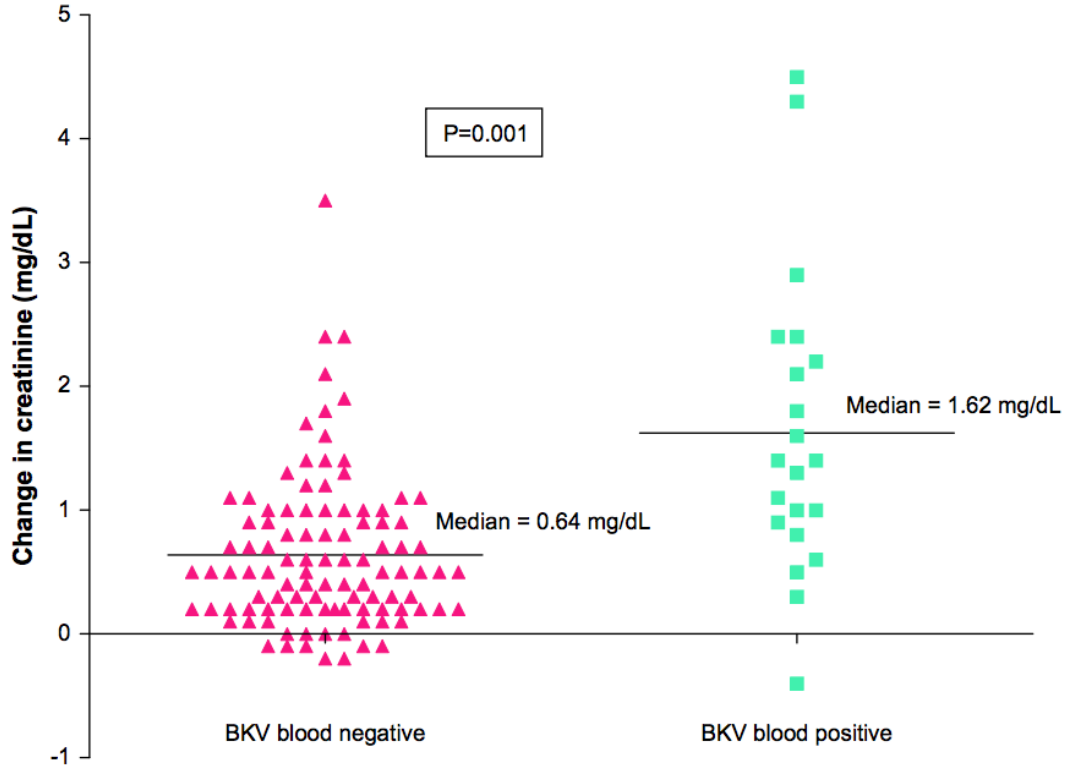




Lee YJ Biol Blood Marrow Transplant. 2014;20:1204

In Allo-HCT, BK Viremia Leads to Renal Dysfunction

- BK viremia in allo-HCT
  - Associated with largest rise in SCr
  - BK viruria precedes viremia



O'Donnell P et al. Biol Blood Marrow Transplant, 2009.

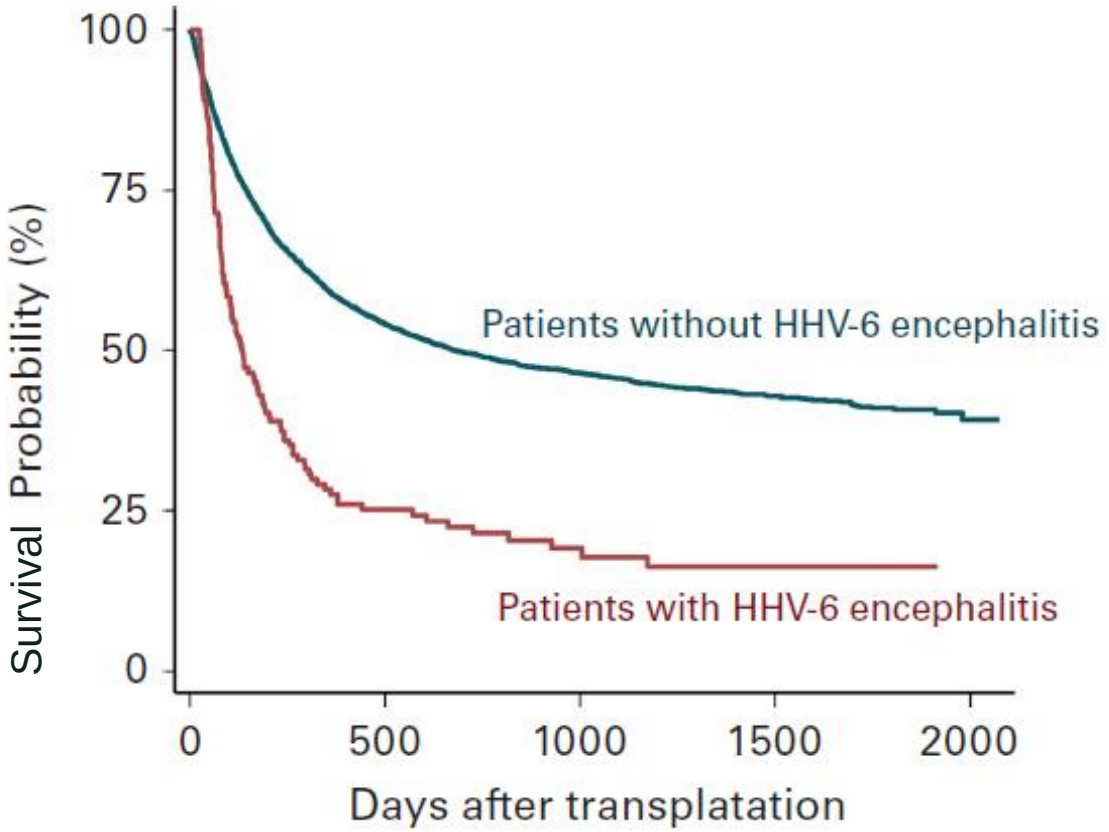
BK Viruria Is Associated with Lower Overall Survival after Allo-HCT

Predictors of mortality	HR (95% CI)
Kidney dysfunction	4.26 (3.69–4.91)
BKV infection	1.27 (1.11–1.44)
High BK viral load 10-fold increase	1.03 (1.02–1.05)
PLT count >50,000	0.47 (0.40–0.54)
Increase in ALC by a factor of two	0.62 (0.60–0.65)

Abudayyeh A et al. Am J Transplant 2016 May;16(5):1492-502.

HHV-6

HHV6 Reactivates Frequently post-HCT



- HHV6 is common: 99% prevalence in western populations
- Reactivation is much more common in cord blood and haplo-HCT
- End-organ disease including encephalitis, graft failure, delayed immune reconstitution, significant impact on memory, are currently underdiagnosed
- HHV6 encephalitis is associated with mortality and long term sequelae in survivors

Ogata et al. BMT 2017

Case Review of Fatal HHV6 Post-HCT

The NEW ENGLAND JOURNAL of MEDICINE

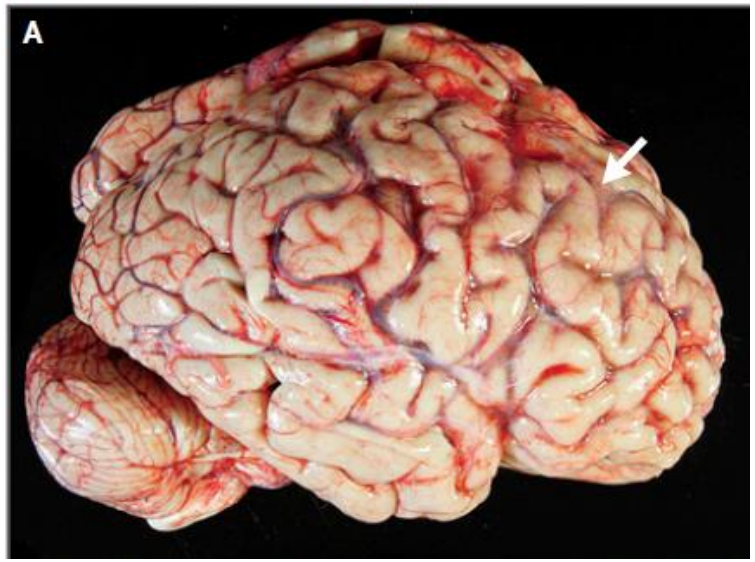
CASE RECORDS of the MASSACHUSETTS GENERAL HOSPITAL

Case 5-2018: A 63-Year-Old Man with Confusion after Stem-Cell Transplantation

Areej R. El-Jawahri, M.D., Pamela W. Schaefer, M.D., Joseph B. El Khoury, M.D.,
and Maria Martinez-Lage, M.D.

N ENGL J MED 378;7 NEJM.ORG FEBRUARY 15, 2018

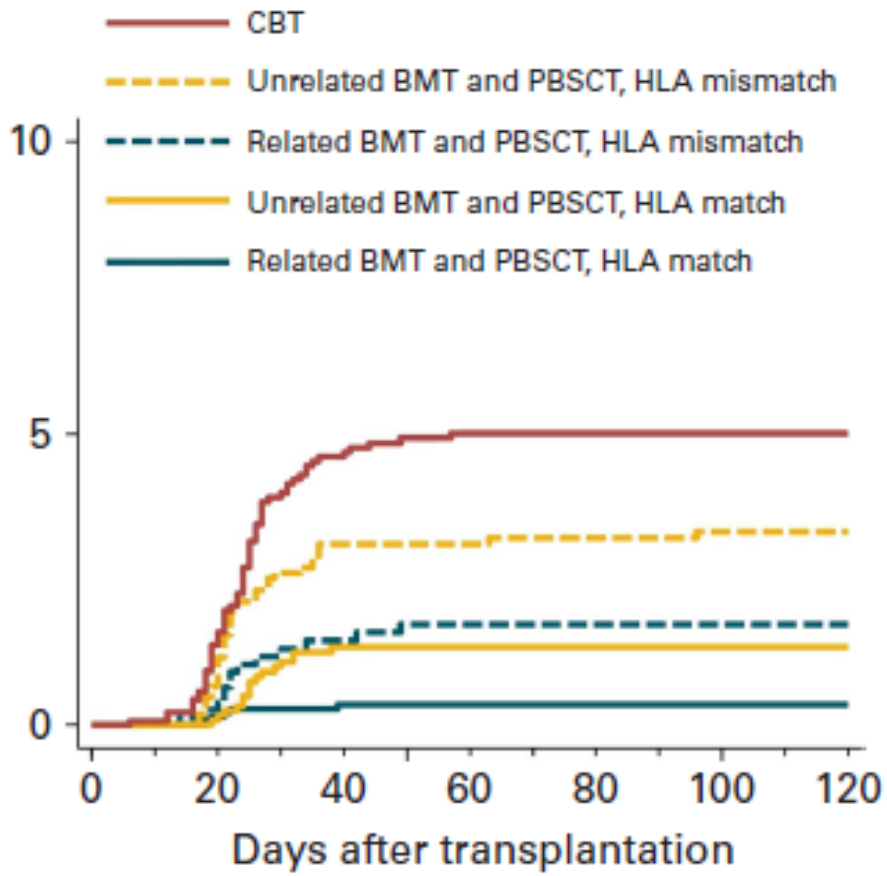
- Recent NEJM case record of a fatal case of post-HCT HHV6 meningoencephalitis, myocarditis, and interstitial nephritis



Management of HHV-6 after HCT is Suboptimal

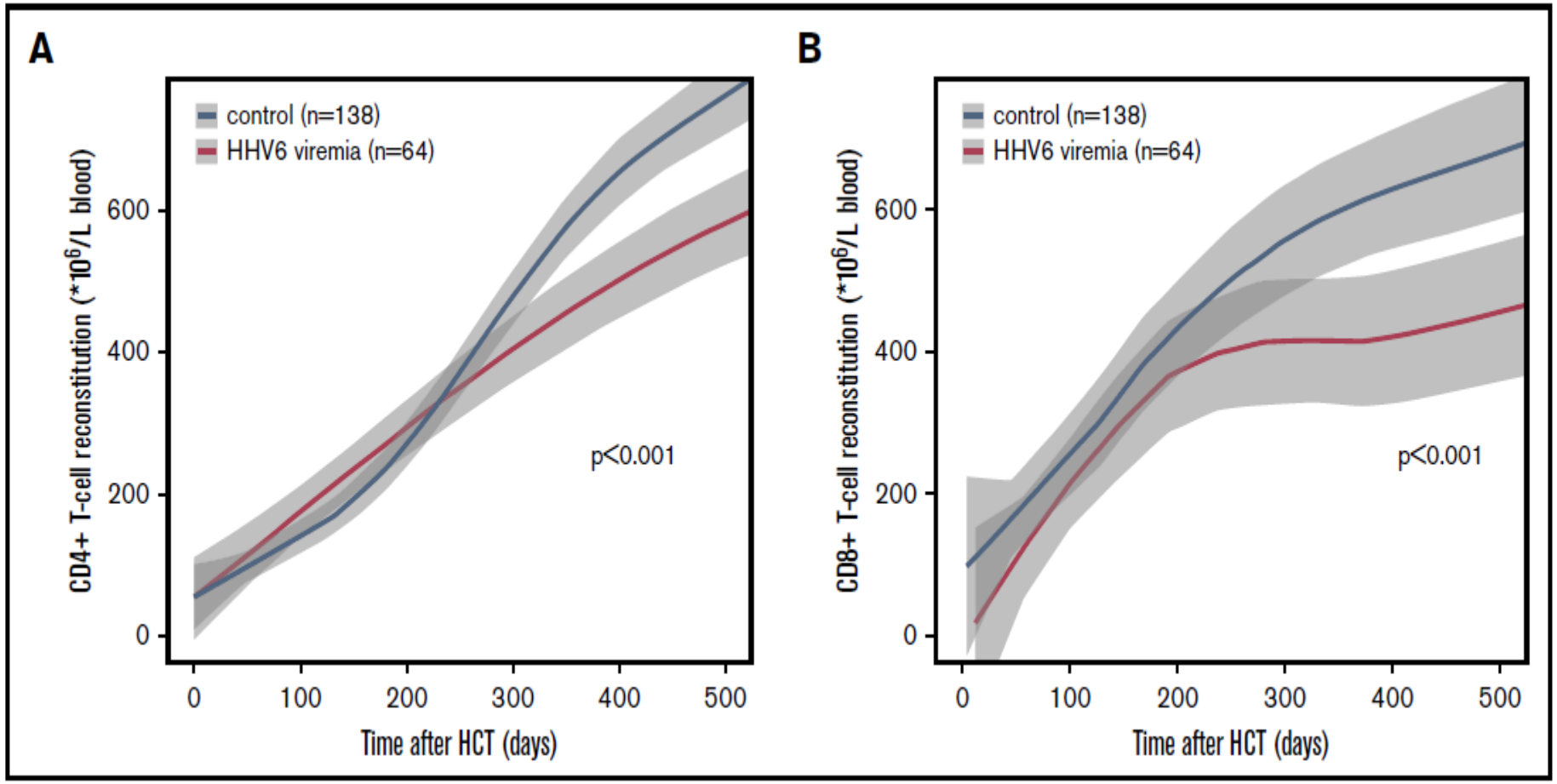
- Retrospective study of 145 Japanese HCT patients with HHV6 encephalitis showed:[1]
  - 71% response to IV GCV, 84% to FOS
    - 57% had persistent neuropsych sequelae
  - 100 day survival: 58% with encephalitis, 81% without
- Foscarnet prophylaxis from day 7-27:[2]
  - Reduced HHV6 viremia (>10^4 c/ml) from 57% in historic controls to 18% (P<0.001)
  - Did not reduce HHV6 encephalitis (**12% with FOS** vs. 5% in historic controls, P=0.14)
  - Concluded that new antiviral agents with better CNS penetration needed

Cumulative incidence of HHV6 encephalitis after HCT in Japan



1 Ogata M et al. BMT 2017;52:1563-70
2 Ogata M et al. BBMT 2018

HHV6 Reactivation Negatively Impact T-cell reconstitution



de Koning C et al.

blood advances 27 FEBRUARY 2018 • VOLUME 2, NUMBER 4

Summary

- Multi-viral infections are common in HCT recipients
- They occur more commonly in high-risk patients (cord blood, haplo, GVHD)
- Multi-viral infection is associated with significant disease and higher mortality
- Drugs and immunotherapies under development could be used to prevent or treat multi-viral infections
  - Brincidofovir:
    - AdAPT study of short-course oral brinci currently enrolling for AdV viremia in children
    - IV BCV in Phase 2: adult HCT recipients with AdV viremia
  - Cellular therapies also under development, but many shortcomings

BCV CLINICAL UPDATES

W. Garrett Nichols, MD, MS
Chief Medical Officer

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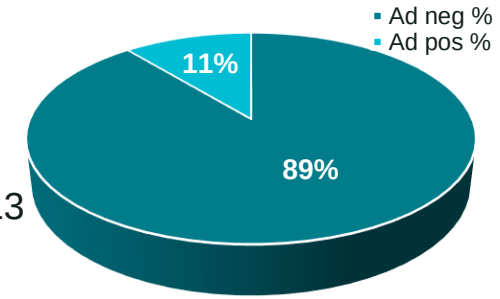
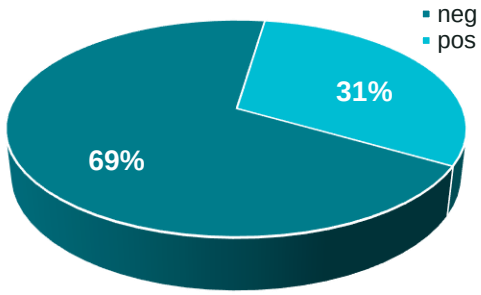
AdV Persists in the Gut of Immunocompetent Children……

143 immunocompetent children: 576 GI biopsies

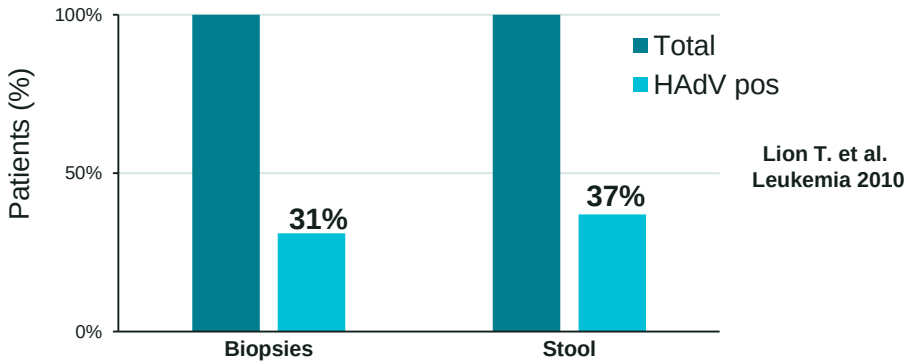
AdV-positive biopsies
pos=63; neg=513



AdV-positive patients
pos=44; neg=99

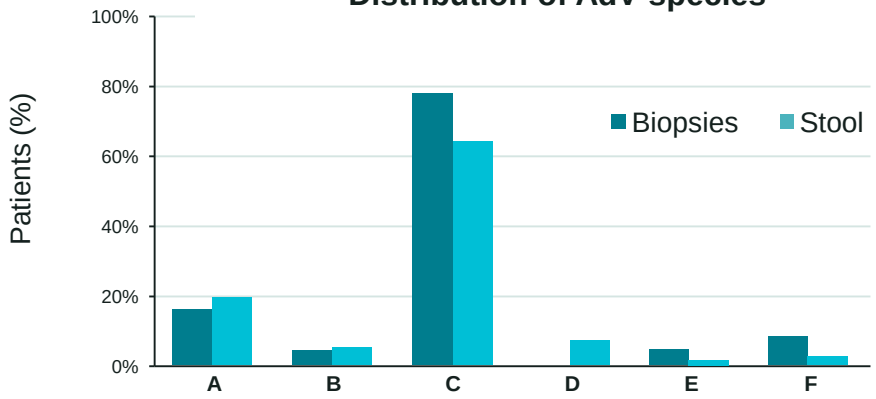


AdV persistence vs reactivation post SCT



Lion T. et al.
Leukemia 2010

Distribution of AdV species



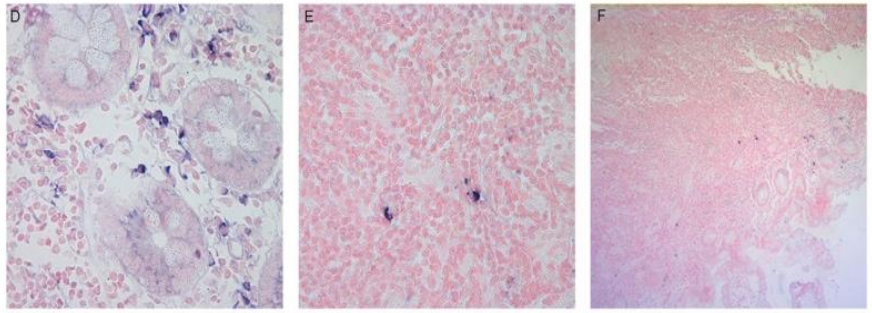
AdV persistence in the GI tract ⟷ risk of reactivation and disseminated disease

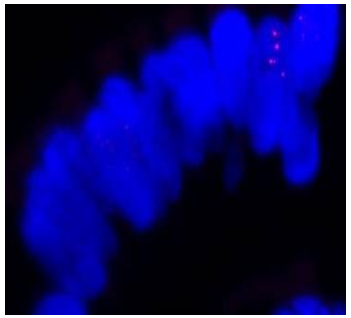
Kosulin K et al. Clin Microbiol Infect 2016, 22(4):381.e1-8

CHIMERIX

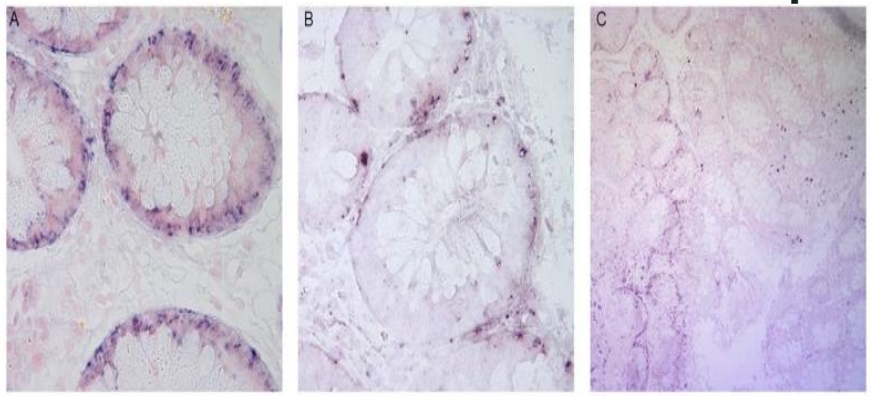
AdV Persists in the Gut of Children……
and Reactivates from the Gut after Transplant

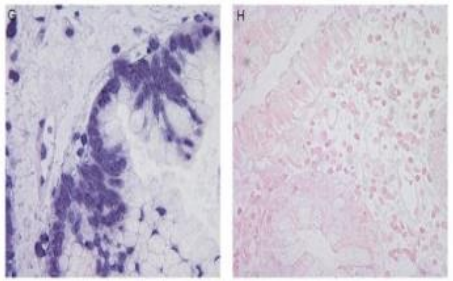
Persistent AdV in gut of immunocompetent children





Reactivated AdV post HCT





positive control negative control

Oral BCV provides targeted therapy for AdV after pediatric HCT:

- **Delivers drug to gut (source of viral replication in pediatric HCT patients)**
- **100-fold greater potency vs. IV CDV**

Kosulin K et al. Clin Microbiol Infect 2016, 22(4):381.e1-8

CHIMERIX

Short-course Oral BCV for Adenovirus: Maximizing the Probability of Success in AdAPT

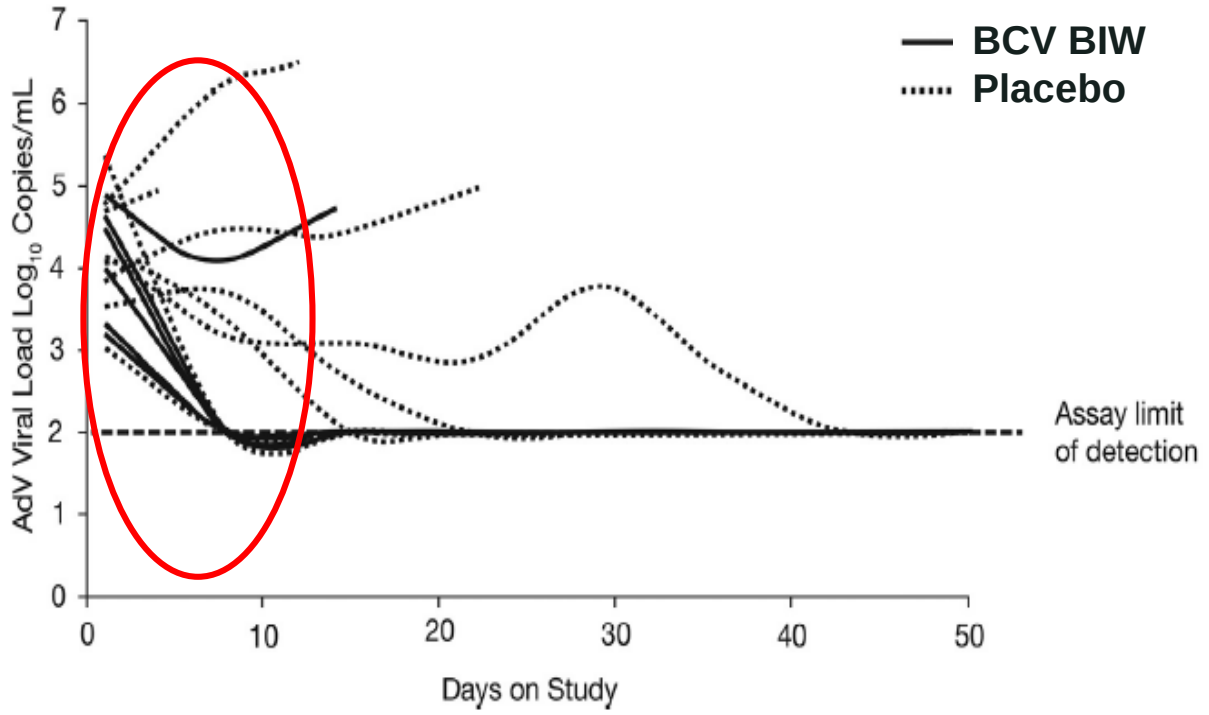
- Rapid identification and treatment of AdV viremia is key:
  - Screening must be conducted at least weekly
  - Intervention with oral BCV as quickly as possible after confirmed viremia enables rapid clearance of AdV from plasma
  - Rapid AdV clearance (week 4) was associated with improved survival in AdVise
- UK cohort: oral BCV had greater virologic effect than IV cidofovir*
  - Robust virologic responses more common with BCV, particularly in first 100 days after HCT
  - Oral BCV was more likely to clear plasma in patients without immune reconstitution
- BCV has demonstrated hematologic safety in early transplant period and has avoided cidofovir-like nephrotoxicity
- Short course oral BCV should improve outcomes compared to off-label IV cidofovir

*Hiwarkar et al. Blood 2017

CHIMERIX

Phase 2 in Asymptomatic AdV: Oral BCV BIW Cleared Plasma in 1 Week if AdV >1000 c/mL

- Study 202 randomized allo-HCT recipients with asymptomatic AdV viremia to oral BCV twice weekly, oral BCV once weekly, or placebo (n=48)
- Learnings included:
  - Low risk (matched sibling recipients of T-cell replete allografts, with AdV < 1000 c/mL) cleared AdV spontaneously
  - Oral BCV twice weekly better than weekly
    - Consistent and more rapid clearance
    - Trend toward improved mortality (vs. QW and PBO)
- AdAPT will enroll high-risk subjects with AdV viremia > 1000 c/mL



Grimley M et al. BBMT 2017;23:512-21

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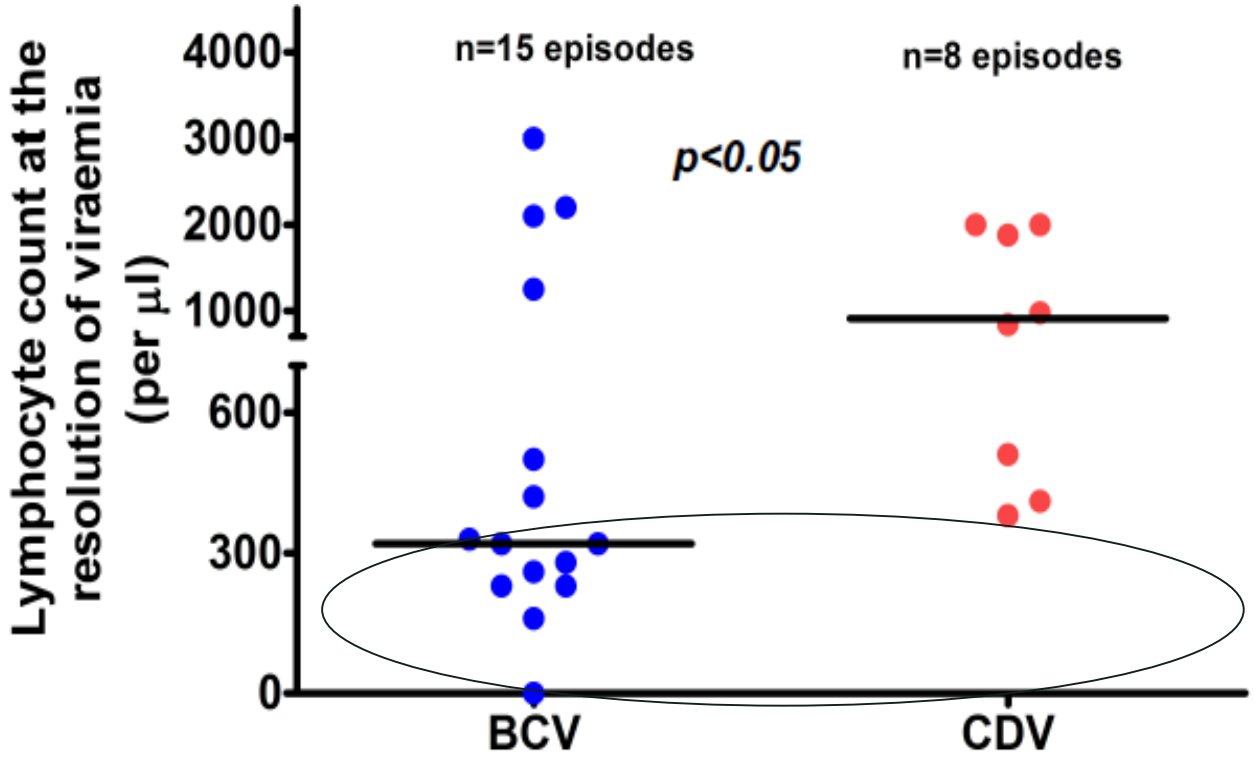
BCV Clears AdV from Plasma with or without Immune Function, While Cidofovir Requires Immune Assistance



- Immune reconstitution: absolute lymphocyte count >300 cells/uL
- T-cell depleted allo-HCT pts have delayed immune reconstitution ~ day 60 or beyond

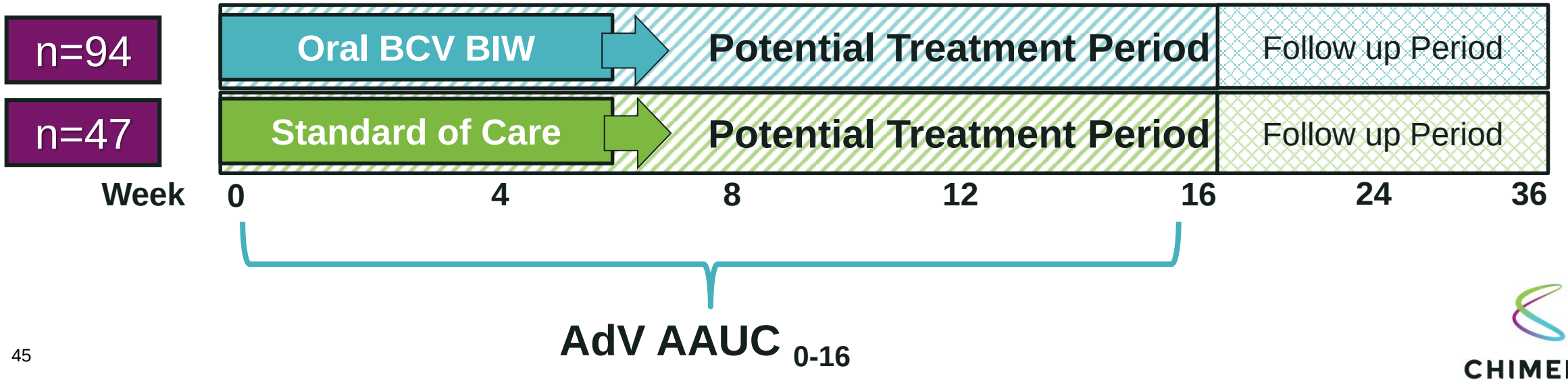
Lymphocyte counts were significantly lower at time of viremia clearance with Oral BCV than with IV CDV

Hiwarkar P et al. Blood 2017 Feb 2. pii: blood-2016-11-749721. doi: 10.1182/blood-2016-11-749721. [Epub ahead of print]

CHIMERIX

AdAPT: Adenovirus after Allogeneic Pediatric Transplantation

- **Open label, comparative study of oral BCV vs. standard of care (SoC) in AdV viremia**
  - Pediatric T-cell depleted allo-HCT recipients in 1st 100 days of HCT with AdV ≥1000 copies/mL
- **Short course pre-emptive therapy**
  - BCV (or SoC) administered until AdV is cleared from plasma
- **Primary endpoint: AdV Average Area Under the Curve over 16 weeks (AdV $AAUC_{0\text{-}16}$)**
  - Powered to detect 0.6 $\log_{10}$ difference in AdV $AAUC_{0\text{-}16}$
- **Small study: N=141 (2:1 randomization)**



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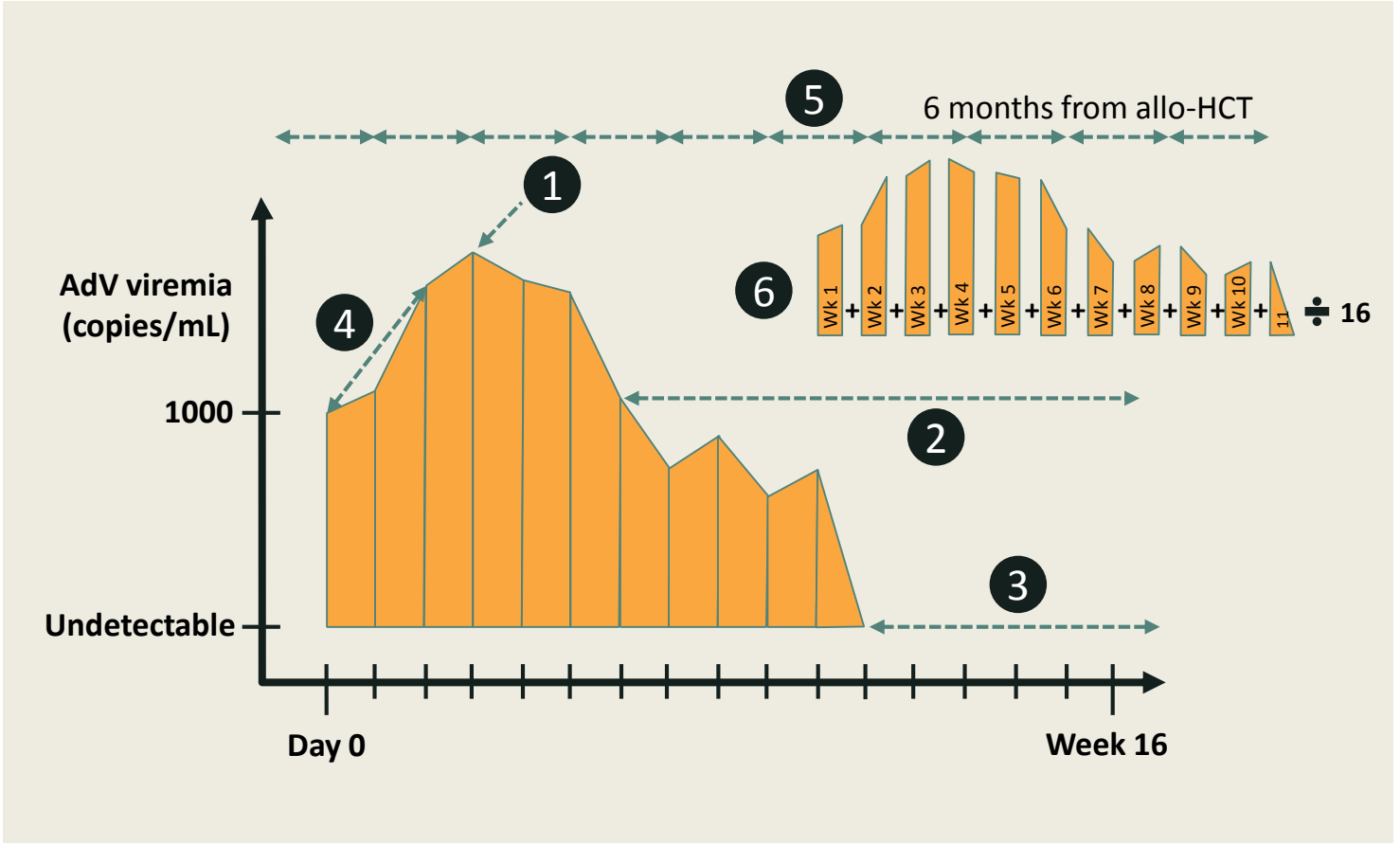
Multiple Measures of AdV Viral Load Are Associated with All-Cause Mortality

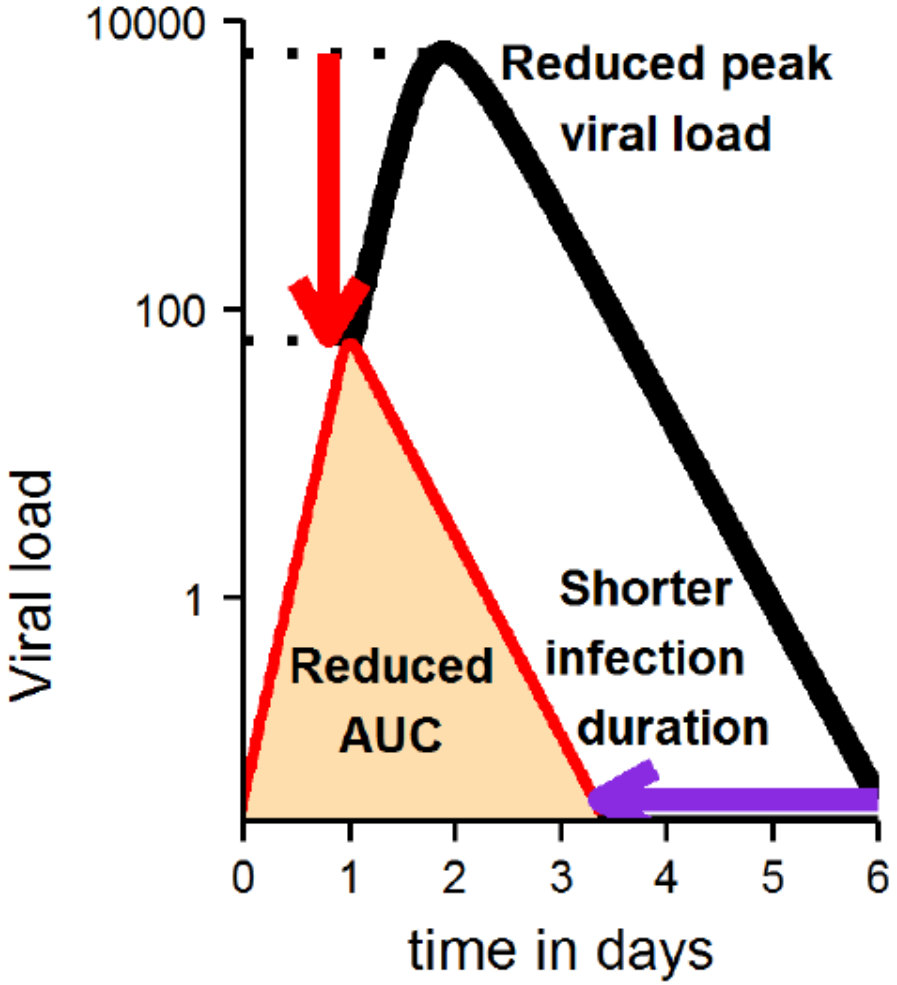
1. **Peak AdV viremia:**
   Peak Log_{10} AdV viremia
2. **Days AdV viremia <1000 copies/mL:**
   Number of days AdV viremia <1000 c/mL
3. **Days undetectable AdV viremia:**
   Number of days AdV viremia <LOD
4. **2-week change in AdV viremia:**
   Change in log_{10} AdV in 2 wks following first AdV viremia ≥1000 copies/mL
5. **AdV viremia over time:**
   Highest log_{10} AdV viremia in 15-day time windows over 6 months following allo-HCT as a time dependent covariate
6. **AdV $AAUC_{0\text{-}16}$:**
   Log_{10} of the time-averaged area under the curve (AdV AAUC)



All measures were over the 16 weeks following first AdV viremia ≥1000 copies/mL, except 2-week change in AdV viremia, and AdV viremia over time

ADVANCE

Measuring Antiviral Activity: Adenovirus Area Under the Curve (AUC)



- Antivirals for acute infections have two major impacts:
  - Decrease peak viral load
  - Shorten time to viral clearance
- Both parameters are captured when measuring viral area under curve (AUC)
- Impact is highest when applied early in the disease course (before peak viral load)
- Assessing viral load over time is most sensitive way to discriminate efficacy between two antivirals

Vegvari C et al. PLoS ONE 11(7): e0158237

CHIMERIX

AdV $AAUC_{0-16}$ Remains the Most Predictive Virologic Measure for All-Cause Mortality

(95% CI)		Peak AdV viremia	Days AdV viremia <1000 c/mL	Days with undetectable AdV viremia	2-week change in AdV viremia	AdV viremia over time	AdV $AAUC_{0-16}$
Hazard for all-cause mortality		**1.31 (1.13 - 1.53)**	**0.96 (0.95 - 0.97)**	**0.96 (0.95 - 0.97)**	**1.24 (1.04 - 1.47)**	**1.37 (1.22 - 1.55)**	**1.91 (1.57 - 2.32)**
Lymphocyte count	≥ 900	1.00	1.00	1.00	1.00	1.00	1.00
	300-899	1.88 [(0.47 - 7.53)	1.82 (0.45 - 7.35)	1.71 (0.43 - 6.89)	1.80 (0.45 - 7.18)	1.64 (0.41 - 6.50)	2.19 (0.54 - 8.86)
	<300	7.81 (2.22 - 27.46)	5.20 (1.48 - 18.32)	5.09 (1.44 - 17.96)	7.97 (2.27 - 27.95)	4.87 (1.35 - 17.52)	6.82 (1.92 - 24.22)
Renal replacement therapy	No	1.00	1.00	1.00	1.00	1.00	1.00
	Yes	13.10 (5.54 - 30.97)	5.09 (1.85 - 14.02)	6.12 (2.21 - 16.98)	14.56 (6.30 - 33.67)	6.90 (2.74 - 17.39)	5.91 (2.38 - 14.72)
AdV disease	No	1.00			1.00		
	Yes	1.79 (0.92 - 3.48)			1.90 (1.00 - 3.63)		
Maximum GvHD stage	0					1.00	
	1,2					0.89 (0.34 - 2.33)	
	3,4					2.31 (1.08 - 4.92)	

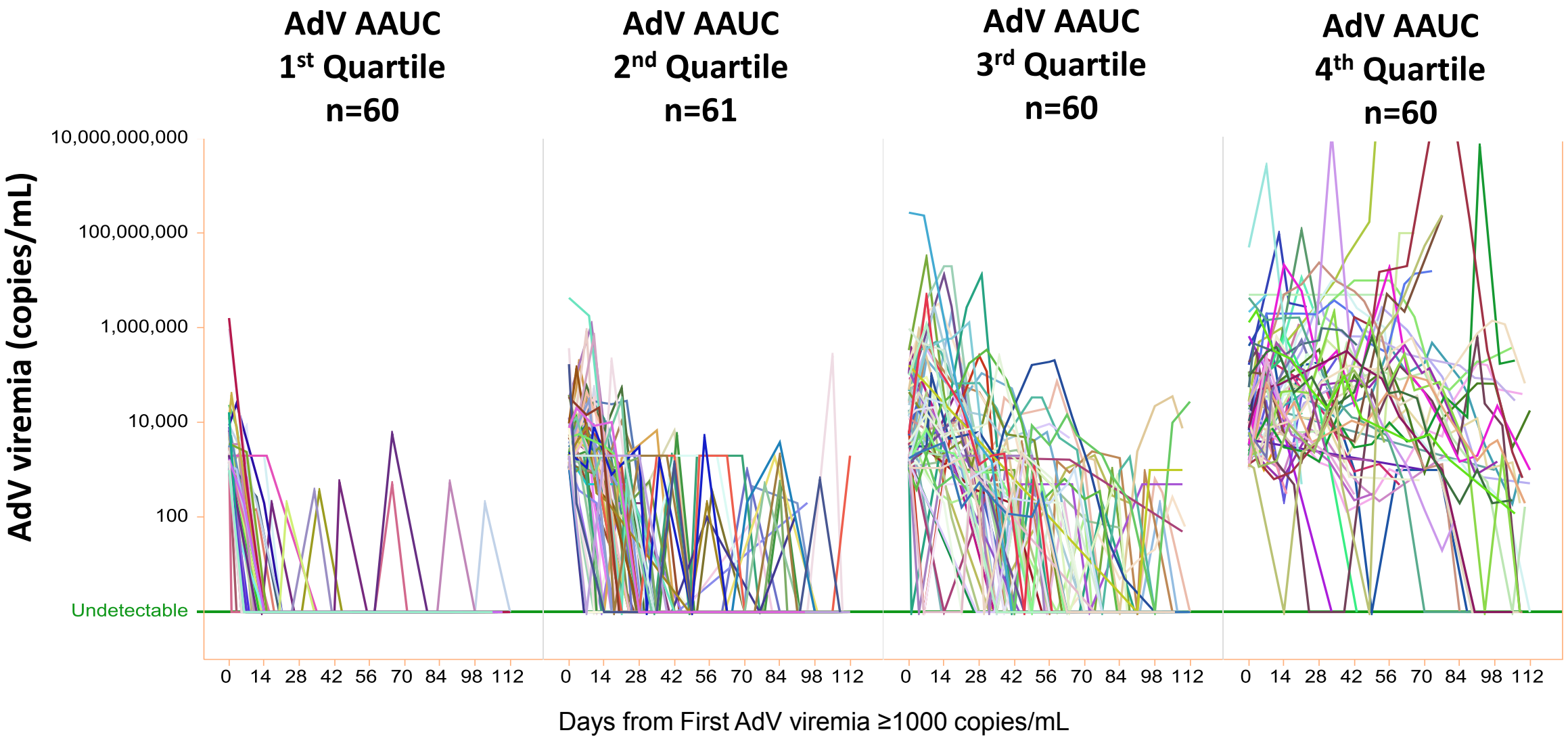
- Associations were independent of lymphocyte immune reconstitution in all models
- Renal replacement therapy (dialysis, possible side effect of IV cidofovir) was also highly correlated with mortality

Galaverna F et al. Presented at ID Week, Oct2018

All models also adjusted for country and patient gender

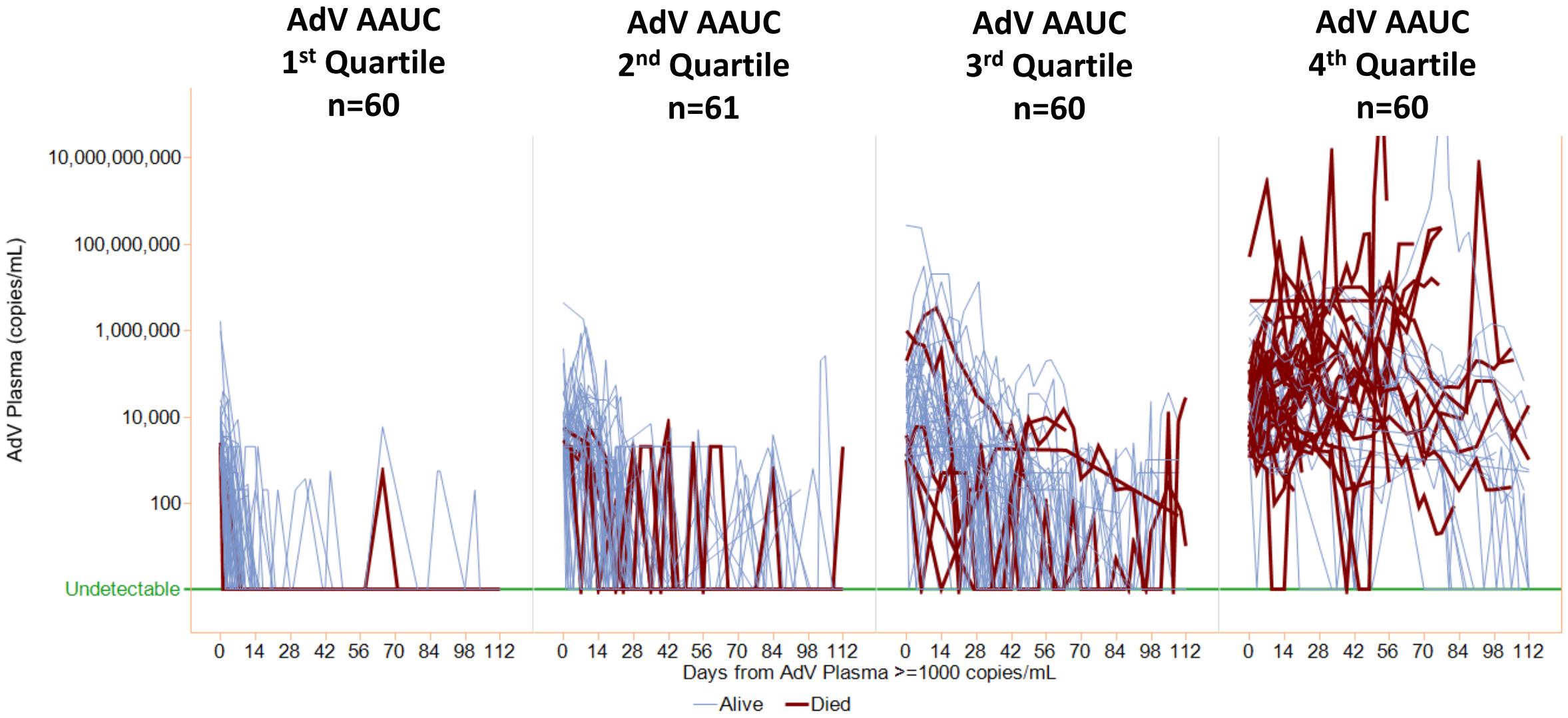
ADVANCE

AdV $AAUC_{0\text{-}16}$ Peak & Persistence = Higher Mortality

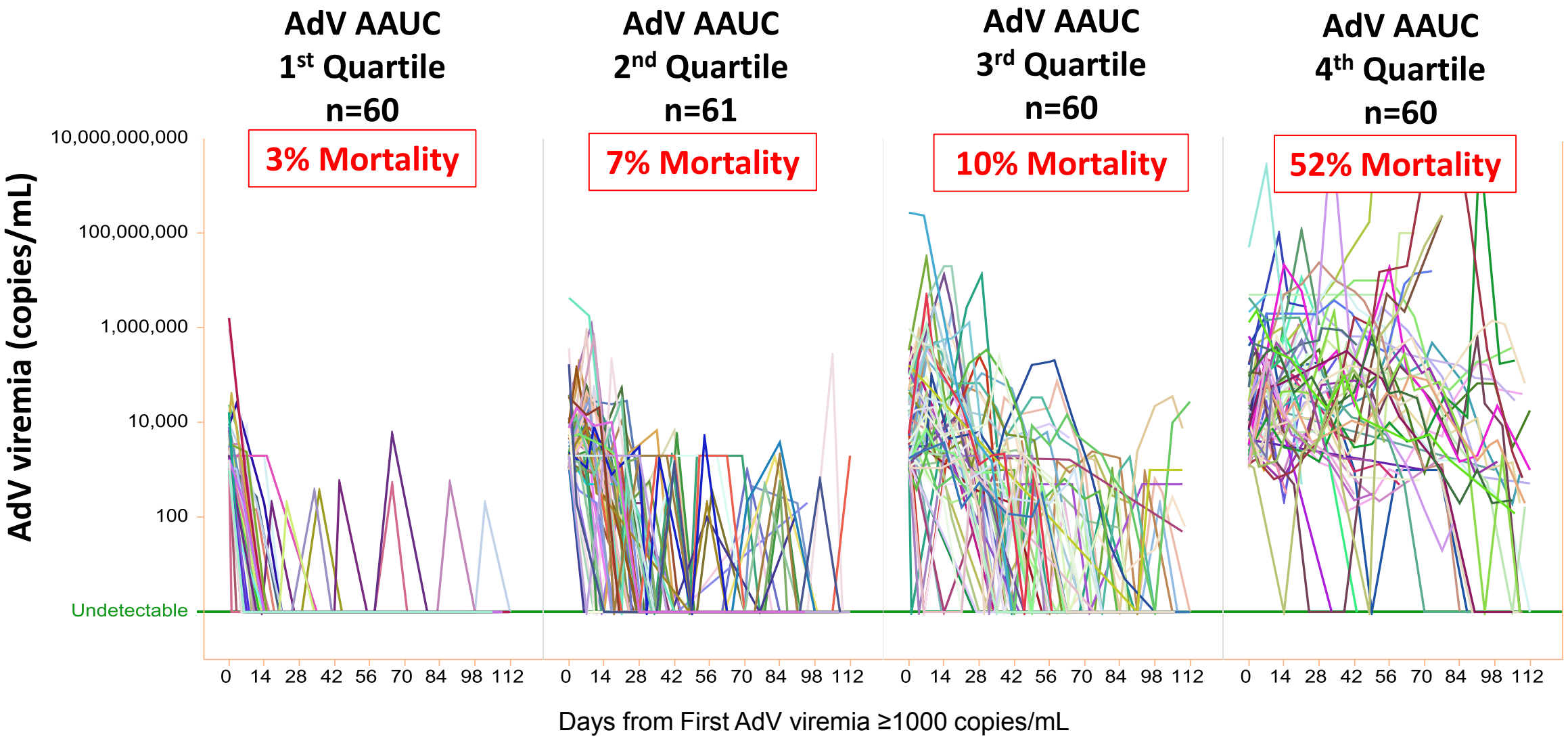


ADVANCE

AdV AAUC0-16 Peak & Persistence = Higher Mortality

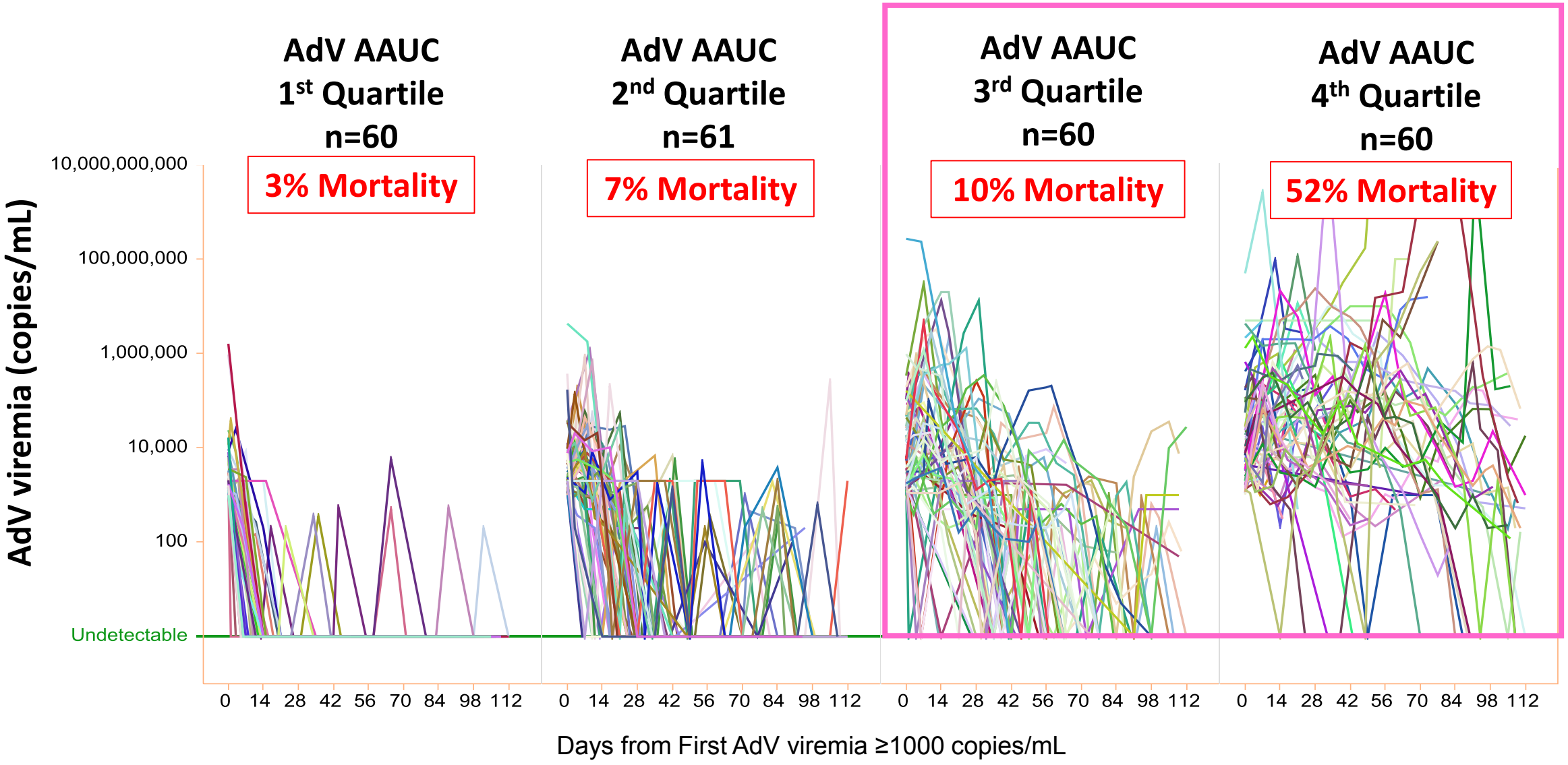


AdV $AAUC_{0\text{-}16}$ Peak & Persistence = Higher Mortality



ADVANCE

AdV $AAUC_{0\text{-}16}$ Peak & Persistence = Higher Mortality



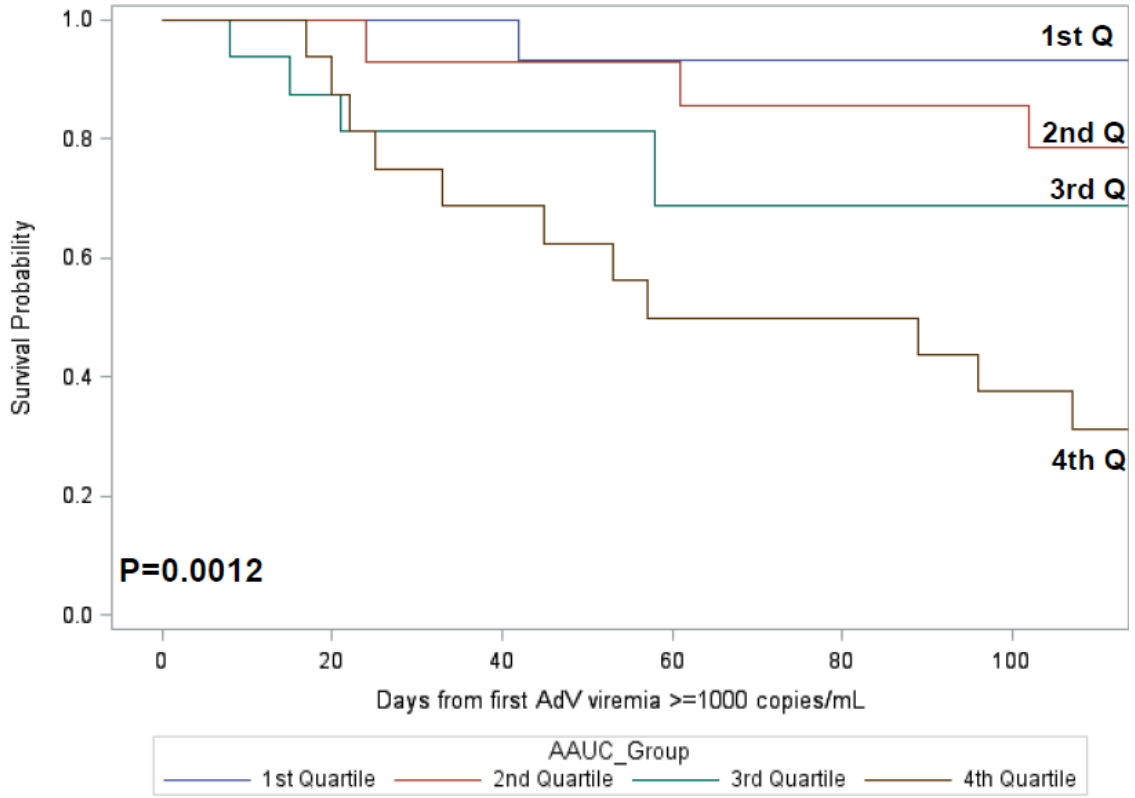
ADVANCE

Two Independent Datasets: Linking AdV Viral Burden and Mortality after HCT

Lion et al: Adenovirus AAUC after Peds HCT Associated with Mortality

Quartile (Range)	Non-relapse Mortality HR (95% CI)	AdV-associated Mortality HR (95% CI)
4th (4.0 – 5.8)	4.4 (2.1 – 9.2)	9.2 (4.3 – 19.9)
3rd (3.3 – 3.7)	2.1 (1.5 – 3.0)	3.0 (2.0 – 4.3)
2nd (2.6 – 3.2)	1.4 (1.2 – 1.7)	1.7 (1.4 – 2.0)
1st (2.1 – 2.3)	Reference (1.0)	

MSKCC: Higher Mortality with Higher AdV Viral Burden after HCT



These data to be published Q4 2018; to be included as supportive independent data sets for Briefing Package for potential Type C meeting to discuss AdV AAUC as surrogate

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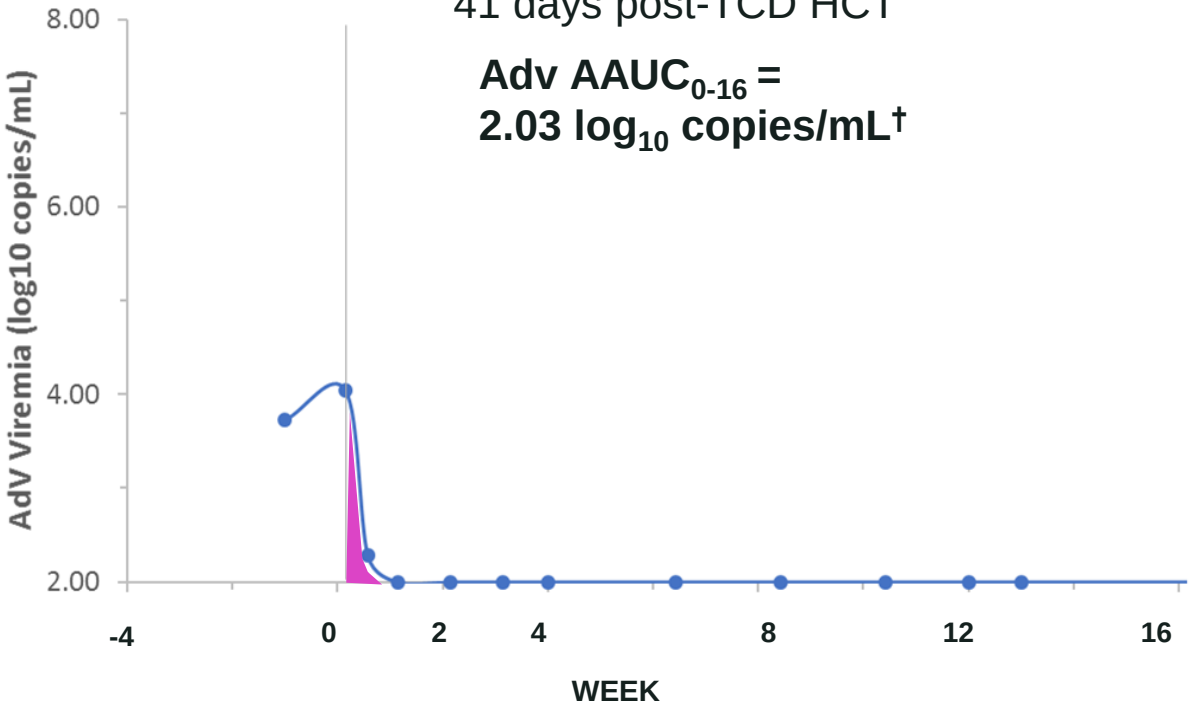
AdAPT Is Designed for Success

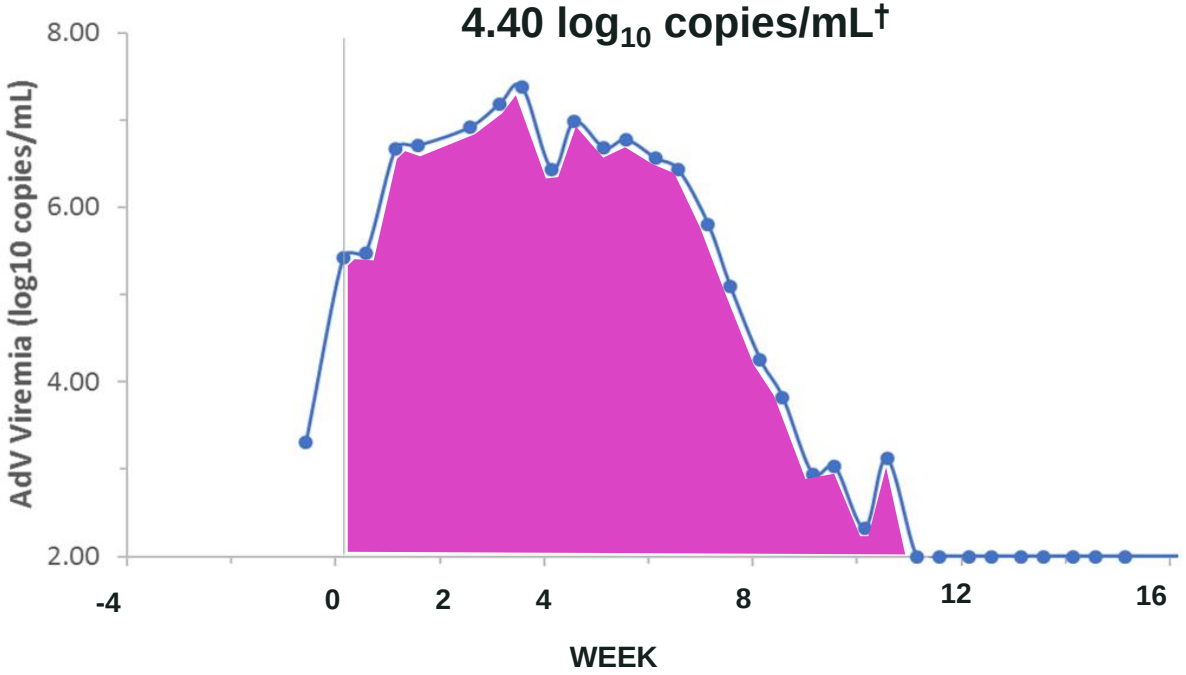
Oral BCV from AdVise
3 yr old pt
41 days post-TCD HCT

Adv $AAUC_{0\text{-}16}$ =
2.03 log_{10} copies/mL†



Local Standard of Care (SoC) from AdVance*
2 yr old pt
19 days post-HCT

Adv $AAUC_{0\text{-}16}$ =
4.40 log_{10} copies/mL†



AdV AAUC for local SOC – AdV AAUC with BCV = potential difference in AdAPT
4.40 - 2.03 = 2.37 log_{10}

*Local standard-of-care may include reduction of immunosuppressants or off-label IV cidofovir
† Lower limit of detection: 2 log_{10} copies/mL

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Acceptance of Virologic Endpoints by US FDA

CMV:

- 2013: CMV Forum established with representatives from academia / industry / regulatory working group
- Meta-analysis conducted on multiple independent data sets, confirmed correlation with clinical endpoints
- Working group reviewed CMV assays to assure consistent results
- October 2017: CMV viremia endpoint accepted by FDA

AdV:

- The Forum is transitioning to include other viral infections in the transplant setting
- AdVance and other independent data sets are being presented/published which demonstrate correlation of AdV virologic markers and clinical outcome

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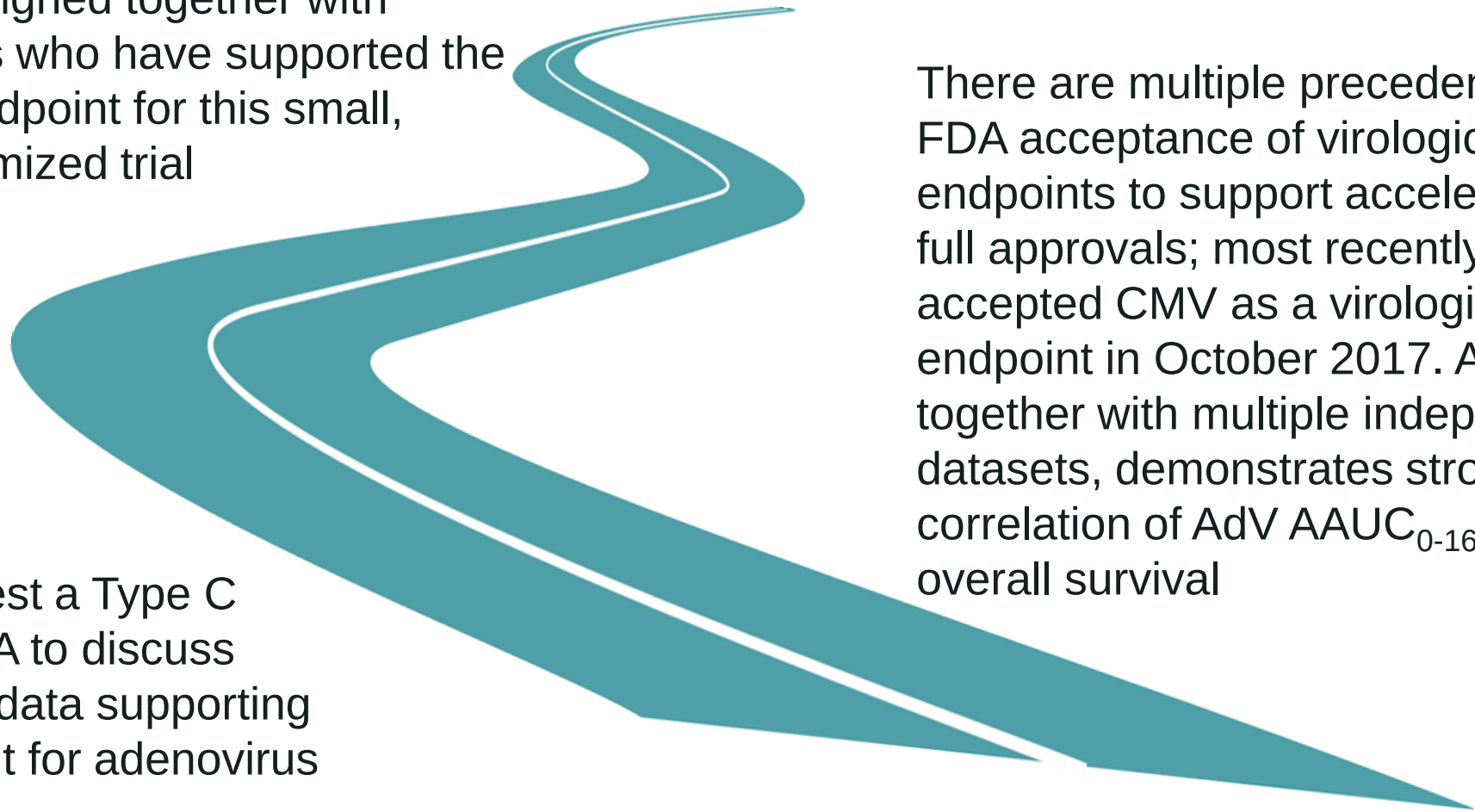
The Path for Approval for Brincidofovir

EU: AdAPT was designed together with European regulators who have supported the use of a virologic endpoint for this small, prospectively randomized trial



There are multiple precedents for FDA acceptance of virologic endpoints to support accelerated or full approvals; most recently, FDA accepted CMV as a virologic endpoint in October 2017. AdVance, together with multiple independent datasets, demonstrates strong correlation of AdV $AAUC_{0\text{-}16}$ with overall survival

We plan to request a Type C meeting with FDA to discuss growing body of data supporting virologic endpoint for adenovirus

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IV BCV May Provide Opportunity to Explore Prevention and Treatment of Other dsDNA Viral Infections

Viral Family	Virus	BCV	Clinical Efficacy Demonstrated in
Adenovirus	Adenovirus (AdV)	0.02	1500+ patients w AdV have received BCV
Polyoma	BK Virus (BKV)	0.13	New data in animal model confirms BCV activity (to be presented at Kidney Week), Ph 2 dose-ranging in planning
	JC Virus (JCV)	0.045	Oral BCV has been used in ~36 pts with PML or JC viremia IV BCV achieves higher CNS penetration
Papilloma	Human Papillomavirus (HPV)	17	BCV used in patients in expanded access trials
Herpes Viruses	Herpes Simplex Virus 1	0.01	BCV cleared acyclovir-resistant HSV-1 after HCT[1]
	Herpes Simplex Virus 2	0.02	BCV cleared acyclovir-resistant HSV-2 after HCT[2]
	Varicella Zoster Virus (VZV, HHV3)	0.0004	BCV demonstrated to prevent shingles post HCT[3]
	Epstein-Barr Virus (EBV, HHV4)	0.03	Anecdotal use in post-HCT viremia and disease
	Cytomegalovirus (CMV, HHV5)	0.001	Antiviral activity demonstrated in Ph 2[4] and Ph 3[5] trials
	Human Herpesvirus 6	0.003	Prevention of viremia and disease in subset analysis of Ph 3 HCT
	Human Herpesvirus 8	0.02	
Pox	Variola	0.1	Ongoing pivotal animal studies in collaboration with BARDA
	Vaccinia	0.8	Disseminated vaccinia cleared with BCV treatment[6]

1. Voight S et al. Transpl Infect Dis 2016;18:791–794
2. El-Haddad D et al. Antiviral Res. 2016;134:58-62.
3. Lee YJ et al. Transpl Infect Dis. 2018 Aug 18:e12977. doi: 10.1111/tid.12977. [Epub ahead of print]
5. Marty FM et al. Biol Blood Marrow Transplant 2016;22(3):S23.
6. Lederman E et al. J Infect Dis. 2012;206:1372-85.

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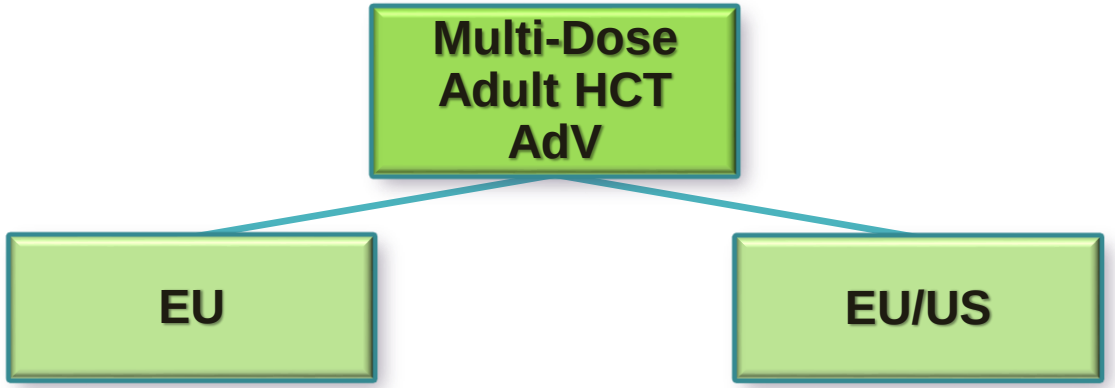
IV BCV in Adult HCT With AdV Viremia: Studies 210/211

Objectives:

- Confirm AdV virologic response with IV BCV in adult HCT patients
- Demonstrate tolerability of IV BCV in patients

Status:

- Multiple countries / sites now initiated for Studies 210/211, additional sites opening in 2H18



Key Design Differences

Study 210	Study 211
UK/Belgium/France/Ireland 13 sites	Italy / US / Spain 13 sites
Patients on cyclosporine	**Patients not on cyclosporine**
2-3 Cohorts ; N = **20-30** 4 doses over 2 weeks	1-2 Cohorts ; N = **10-20** 4 doses over two weeks
UK, Belgium CTAs approved	IND Approved; CTAs Approved

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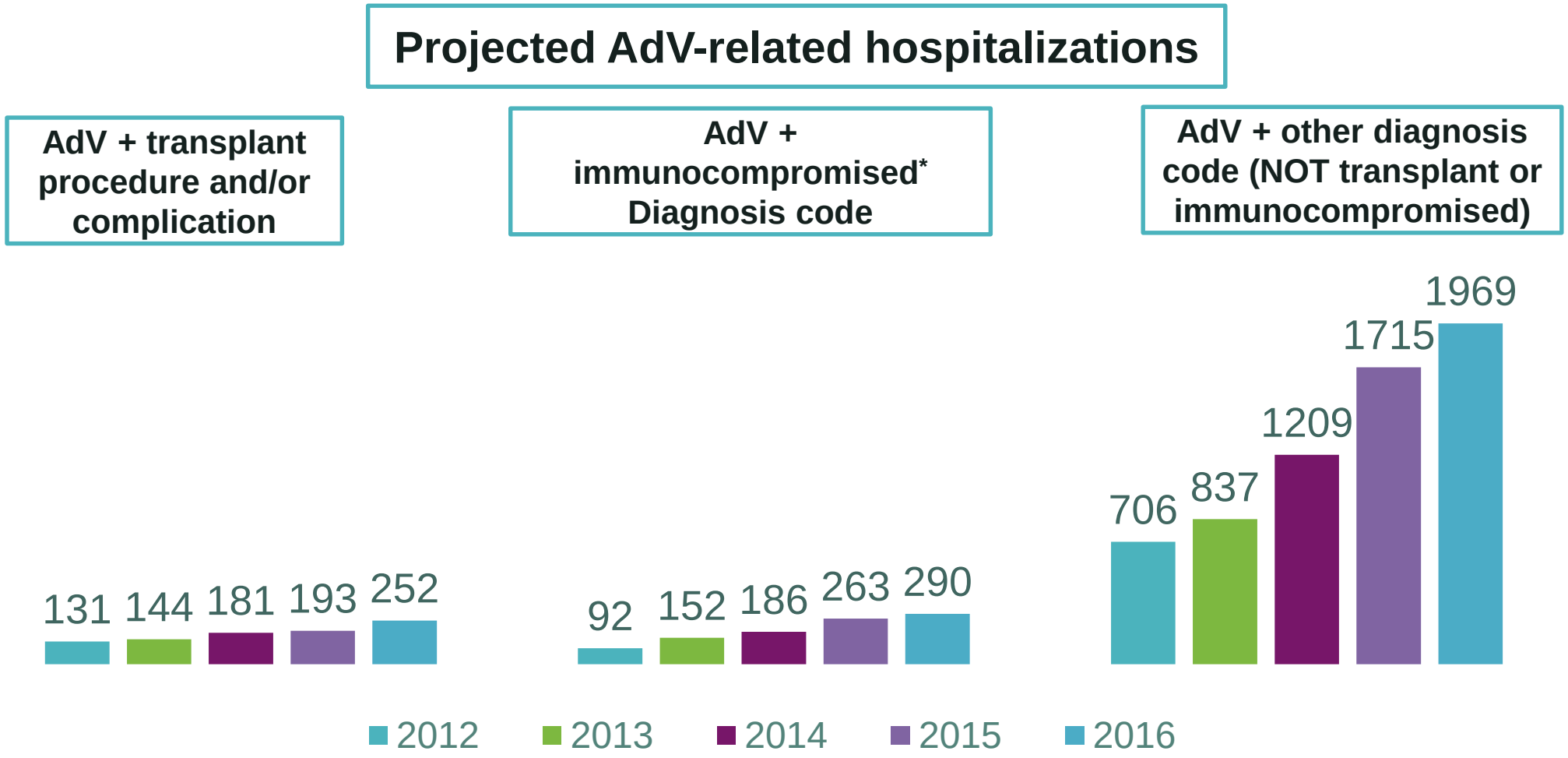
If Accelerated Approval Achieved with AdAPT, IV BCV Could Be Explored in Additional AdV Prevention or Treatment Scenarios

- The lower risk of GI toxicity with IV BCV may allow longer duration of dosing throughout high-risk period
- Pediatric patients are at high risk for multiple DNA virus infections, with adenovirus-related mortality a particular concern
  - High-level detection of AdV in stool predicts AdV disease after peds allo-HCT[1]
- MVP-Peds: **placebo-controlled trial of IV BCV in pediatric allo-HCT recipients** with AdV detected in stool
  - Primary endpoint of prevention of adenovirus disease allows placebo control
  - Secondary endpoint of prevention of CMV, as high-risk pediatric HCT recipients tend to reactivate AdV earlier than CMV
  - Other secondary endpoints to include prevention of other DNA virus and health outcomes

[1] Hiwarkar P et al. Rev Med Virol. 2018 May;28(3):e1980

CHIMERIX

HCUP: Most U.S. AdV-related Hospitalizations are NOT in Transplant Recipients or Immunocompromised Patients



*AdV+immunocompromised exclude those hospitalizations with discharge diagnoses of "transplant" or "post-transplant complication"

NIS sample is 20%, projected numbers have been multiplied by 5

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~12,000 Pediatric Hospitalizations for AdV Annually

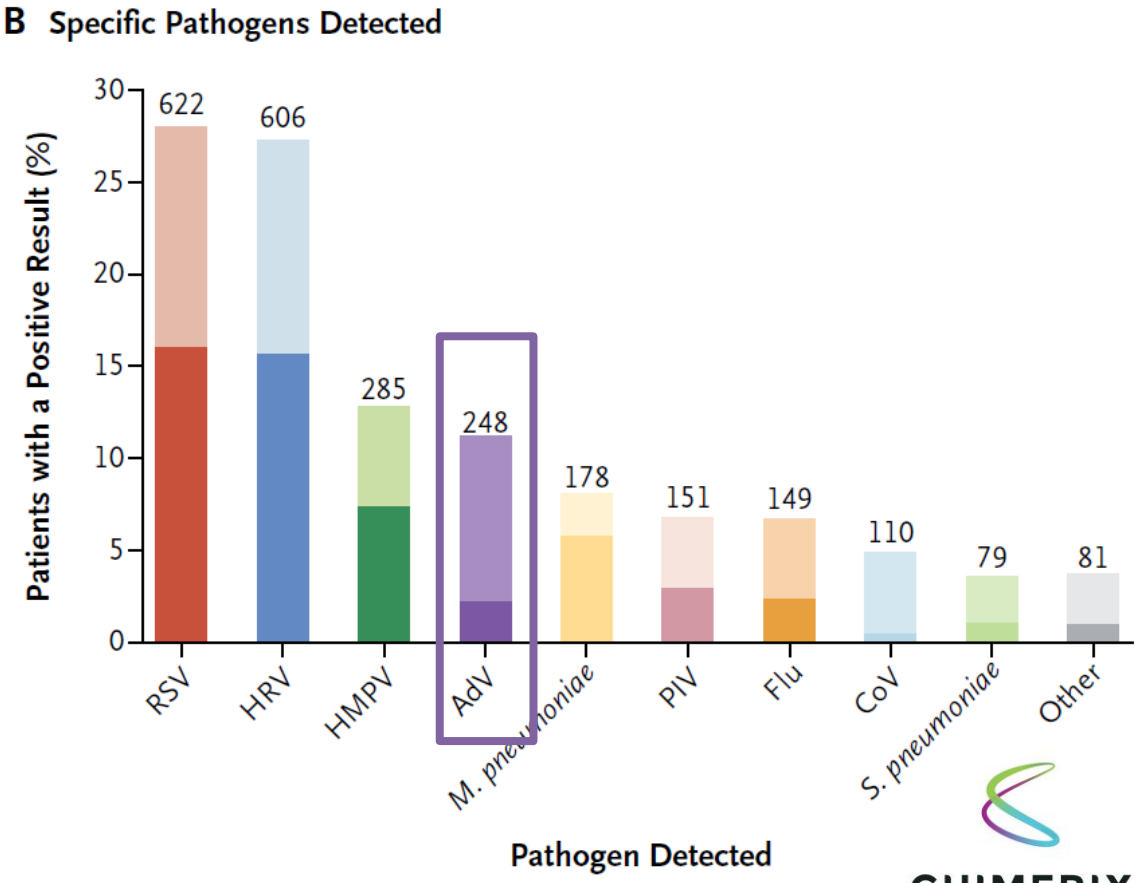
- 2,638 eligible children enrolled
  - 51% had underlying condition (asthma 33%, preterm 21%)
  - 21% required intensive care, and 3 (<1%) died
- Pneumonia: 15.7 cases per 10,000 children
- **Adenovirus was detected in 11%**
  - More common among younger children <5 yo (15%) vs. ≥ 5 yo (3%)
- **Hospitalized AdV pneumonia occurs in 1.6 per 10,000 kids in US annually:**
  - **~12,000 cases per year**

N Engl J Med 2015; 372: 835-45. DOI: 10.1056/NEJMoa1405870

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Community-Acquired Pneumonia Requiring Hospitalization among U.S. Children



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LAND with AdAPT

Multiple Options for EXPAND

2019

Land

- AdAPT

  +

- Smallpox

IV BCV:

- ❑ Complete Studies 210/211
- ❑ 3b/4 study of AdV in hospitalized pts
- ❑ Dose confirmation for younger age groups
- ❑ Dose range finding in BKV (kidney transplant recipients)

Expand

- HHV6 or other CNS viral infection
- BKV if supported by Phase 2 study

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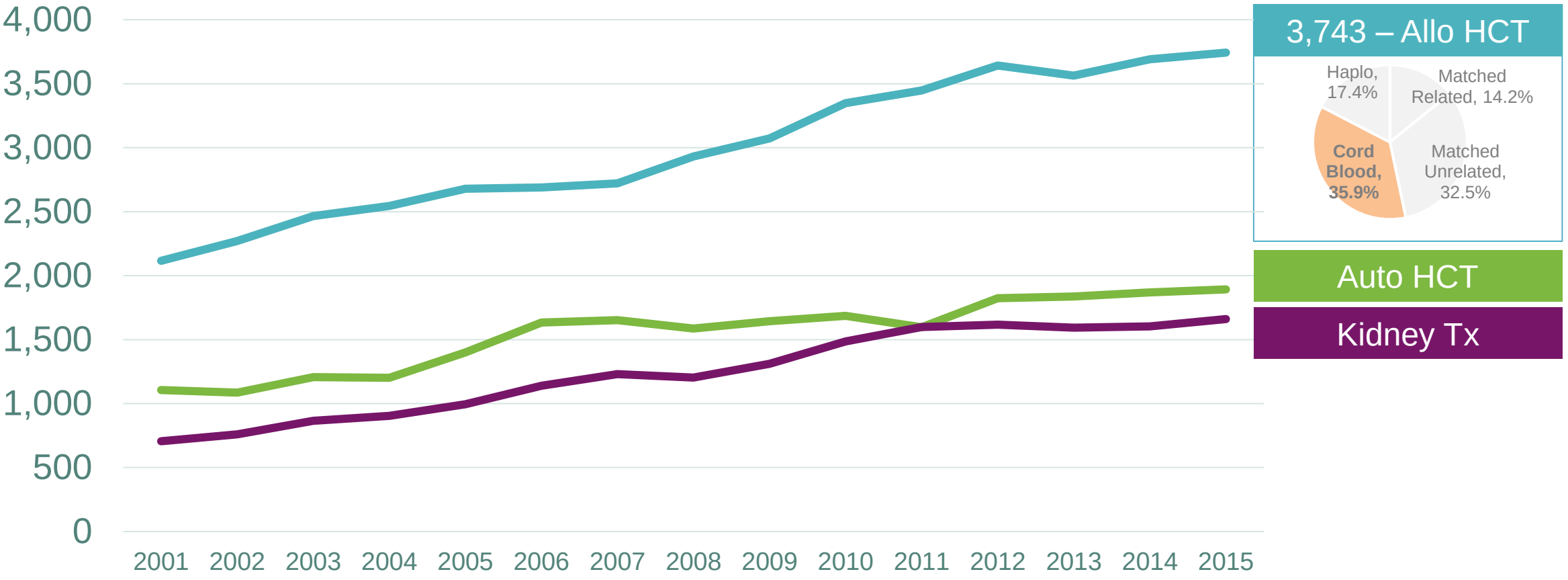
Considering Ex-US/EU Opportunities: Higher Number of Cord Blood Transplants in Japan than in US



Japan Society for Hematopoietic Stem Cell Transplantation, Japanese Society for Clinical Renal Transplantation

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Brincidofovir: Potent Activity Against HHV6

Viral Family	Virus	BCV	Cidofovir	Maribavir	Letermovir	Ganciclovir*	Foscarnet	Acyclovir
Adenovirus	Adenovirus (AdV)	0.02	1.3	—	>10	4.5-33	Inactive	>100
Polyoma	BK Virus (BKV)	0.13	115	—	—	>200	Inactive	>200
	JC Virus (JCV)	0.045	>0.1	—	—	—	Inactive	—
Papilloma	Human Papillomavirus (HPV)	17	716	—	—	Inactive	—	Inactive
Herpes Viruses	Herpes Simplex Virus 1	0.01	3.0	Inactive	>10	0.7	92-95	3.8
	Herpes Simplex Virus 2	0.02	6.5	Inactive	>10	2.5	91-96	4.4
	Varicella Zoster Virus (VZV, HHV3)	0.0004	0.5	Inactive	>10	1.3	39.8	3.6
	Epstein-Barr Virus (EBV, HHV4)	0.03	65.6	0.63	>10	0.9	<500	6.2
	Cytomegalovirus (CMV, HHV5)	0.001	0.4	0.31	0.005	3.8	50-800	>200
	Human Herpesvirus 6	0.003	2.7	Inactive	>10	5.8	16	10
	Human Herpesvirus 8	0.02	2.6	Inactive	—	8.9	177	>100
Pox	Variola	0.1	27	—	—	—	—	—
	Vaccinia	0.8	46	—	—	>392	Inactive	>144

Potency expressed as EC_{50} = concentration in µM required to reduce viral replication by 50% *in vitro;* "—" indicates no data.
*Valganciclovir is rapidly converted to ganciclovir *in vivo*; ganciclovir is the relevant compound for cell activity studies.
Source: Data are compiled from multiple sources and include multiple materials and methodologies.

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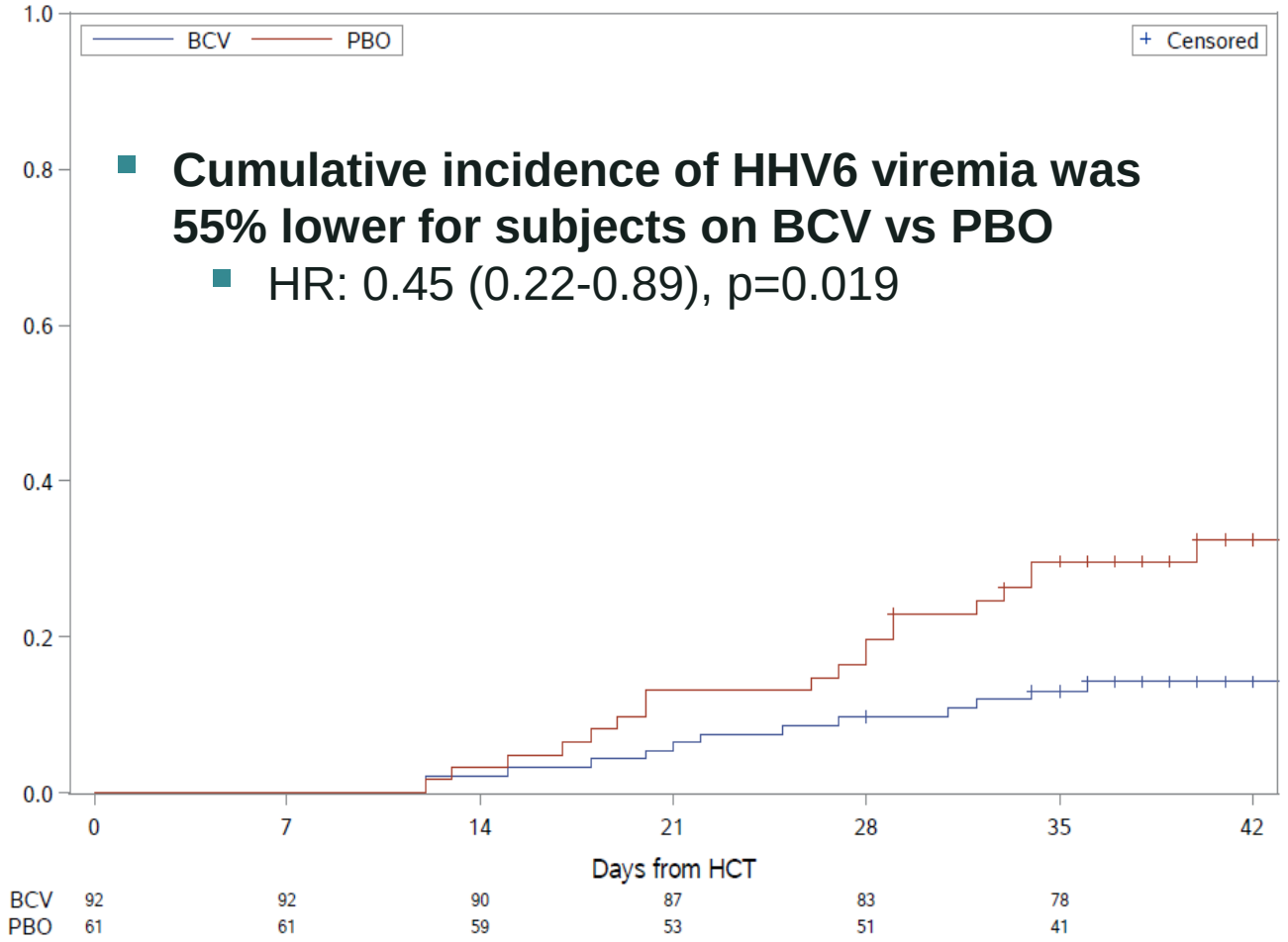
New Data: Oral BCV Prevented HHV6 Viremia and Disease

- An analysis of HHV6 was conducted on plasma from SUPPRESS subjects who:
  1) Started blinded study drug in the first 2 wks post-HCT and
  2) Received at least 3 wks BCV or PBO
- BCV n=92 vs PBO n=61
- Cumulative incidence of HHV6 viremia through week 6:
  - BCV: 14/92 = 15%
  - PBO: 19/61 = 31%



Chimerix internal data

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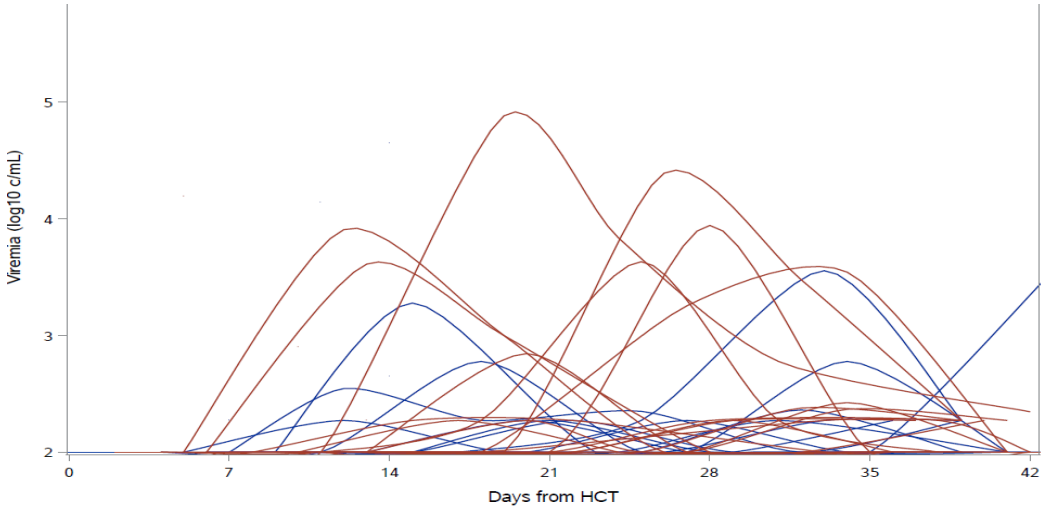
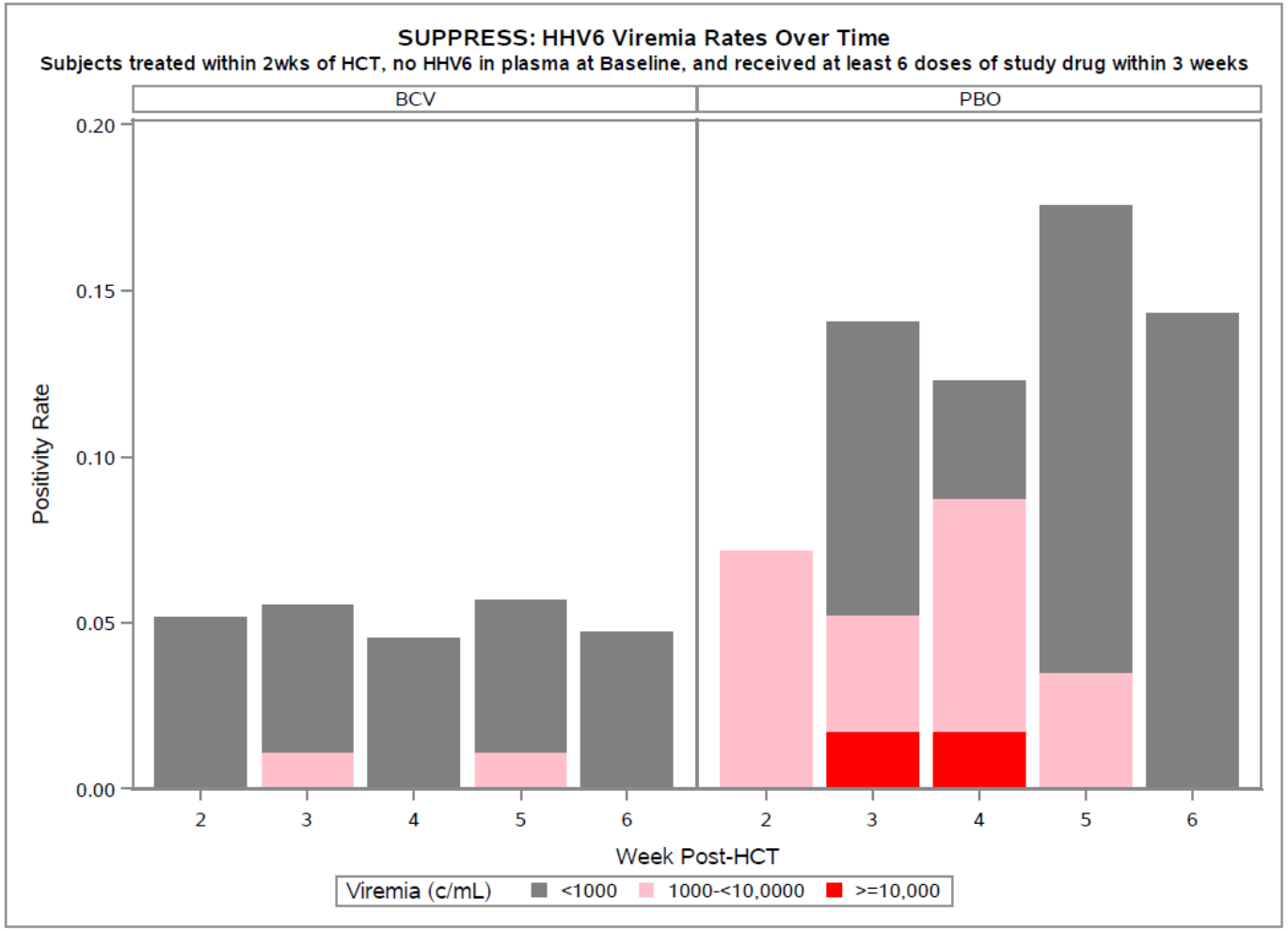
New Data: Oral BCV Significantly Reduced HHV6 Viremia

- For subjects reactivating HHV6, viral loads were lower in those on BCV (blue) compared to those on PBO (red)
- **HHV6 Viremia >1000 c/mL:**
  - **BCV: 2/92 = 2%**
  - **PBO: 7/61 = 11%**
- **HHV6 encephalitis** confirmed in **1/149 PBO** recipients vs **0/303 BCV** recipients





Chimerix internal data

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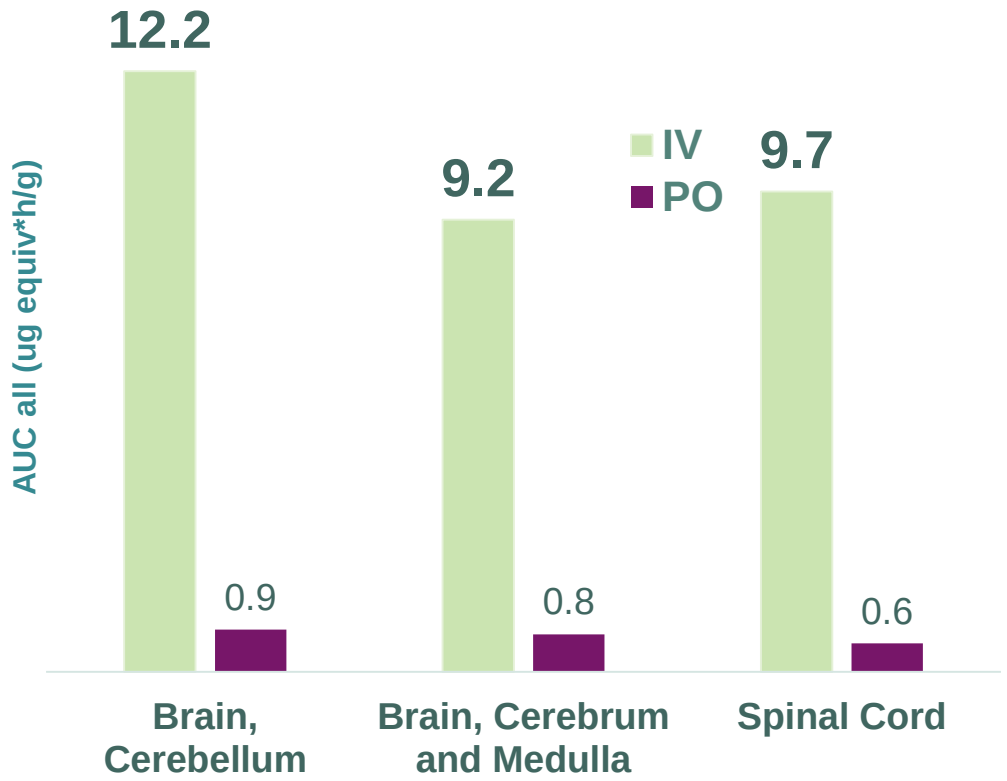
IV BCV: Animal Studies Show More BCV in Difficult-to-reach Compartments Including the Brain

Total Drug Exposure (AUC_{all}) in CNS Tissues (rats)



Points to Note

- Higher CNS exposures with IV BCV supports testing for viral infections in the brain, e.g.:
  - HSV encephalitis in newborns and adults
  - **HHV6 encephalitis**
  - JC virus/PML in transplant recipients or patients with Multiple Sclerosis

Higher drug levels of BCV achieved with IV administration supports evaluation of IV BCV for viral brain infections, such as HHV6 encephalitis or JC virus (PML)

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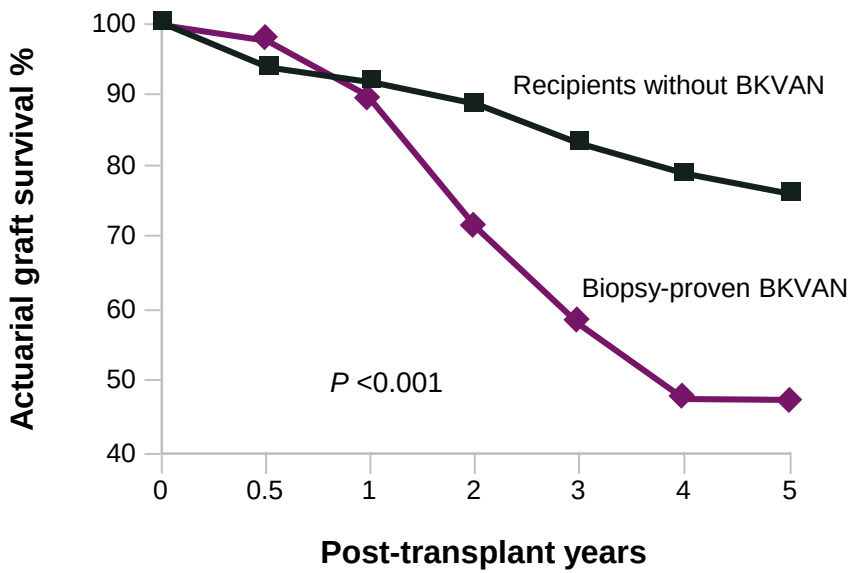
BKV Nephropathy In Kidney Transplant Often Results in Graft Loss

- BKV-associated nephropathy (BKVAN) occurs in up to10% of kidney recipients, with irreversible renal dysfunction in up to 50% of these patients
- Only options currently are return to dialysis (~$75K/yr) or repeat transplant (>$250K)

Actuarial renal graft survival in renal recipients with or without BKVAN[3]



	WITH BKVAN (N=41)	WITHOUT BKVAN (N=960)
6 months	97%	94%
1 year	90%	92%
3 years	58%	83%
5 years	47%	76%

A total of 1001 renal and renal/pancreas transplants were performed at a single center between January 1996 and December 2003, with follow-up through September 2004. 41 cases of BKVN were diagnosed during the study period. 1. Hu JH, et al. *Transplant Proc.* 2011;43:3715-3719; 2. Hirsch HH, et al. *Am J Transplant.* 2013;13:179-188; 3. Vasudev B, et al. *Kidney Int.* 2005;68:1834-1839.

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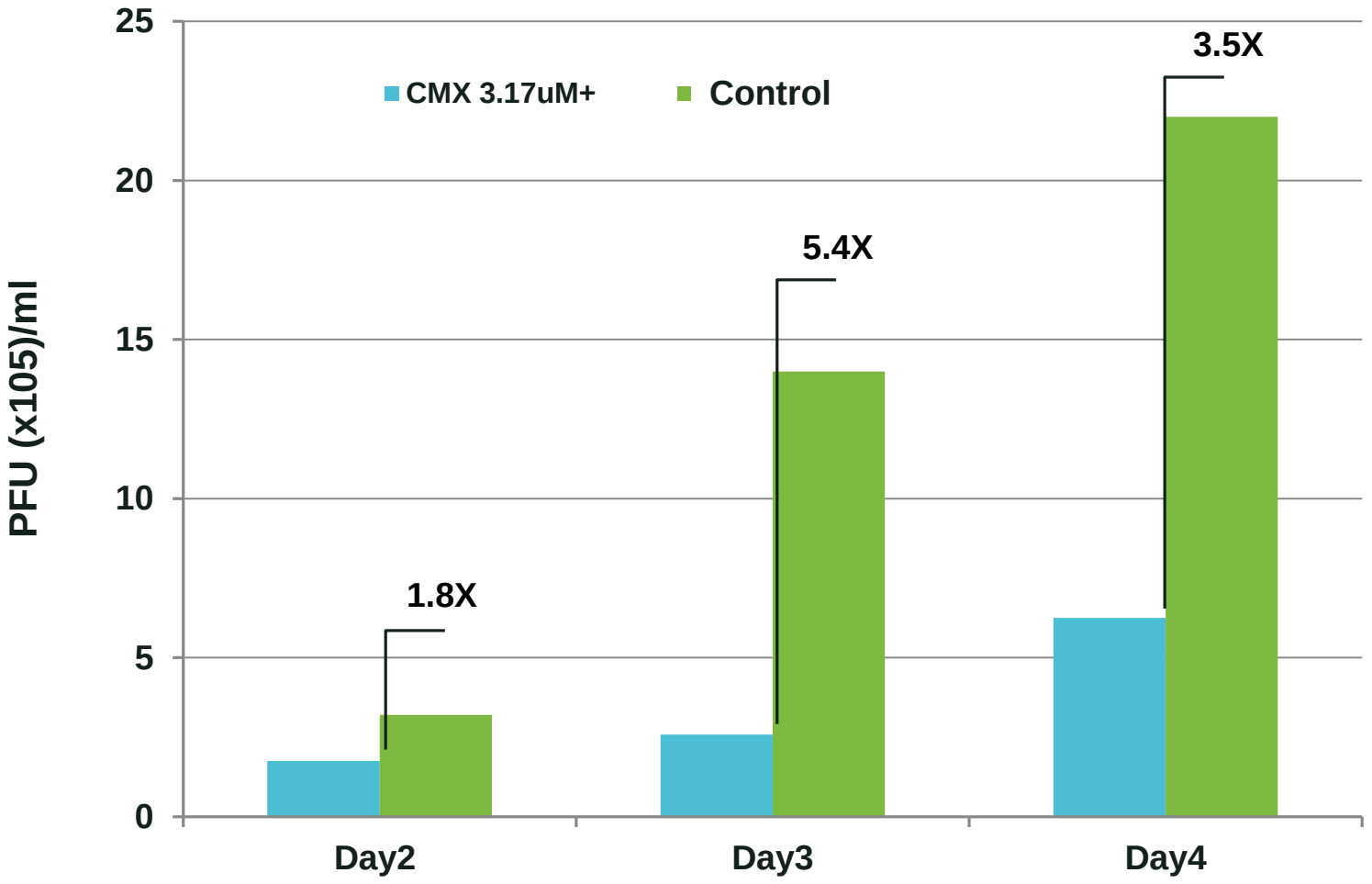
New *In Vitro* Data: BCV Reduced Mouse Polyoma Virus Replication



Chimerix internal data

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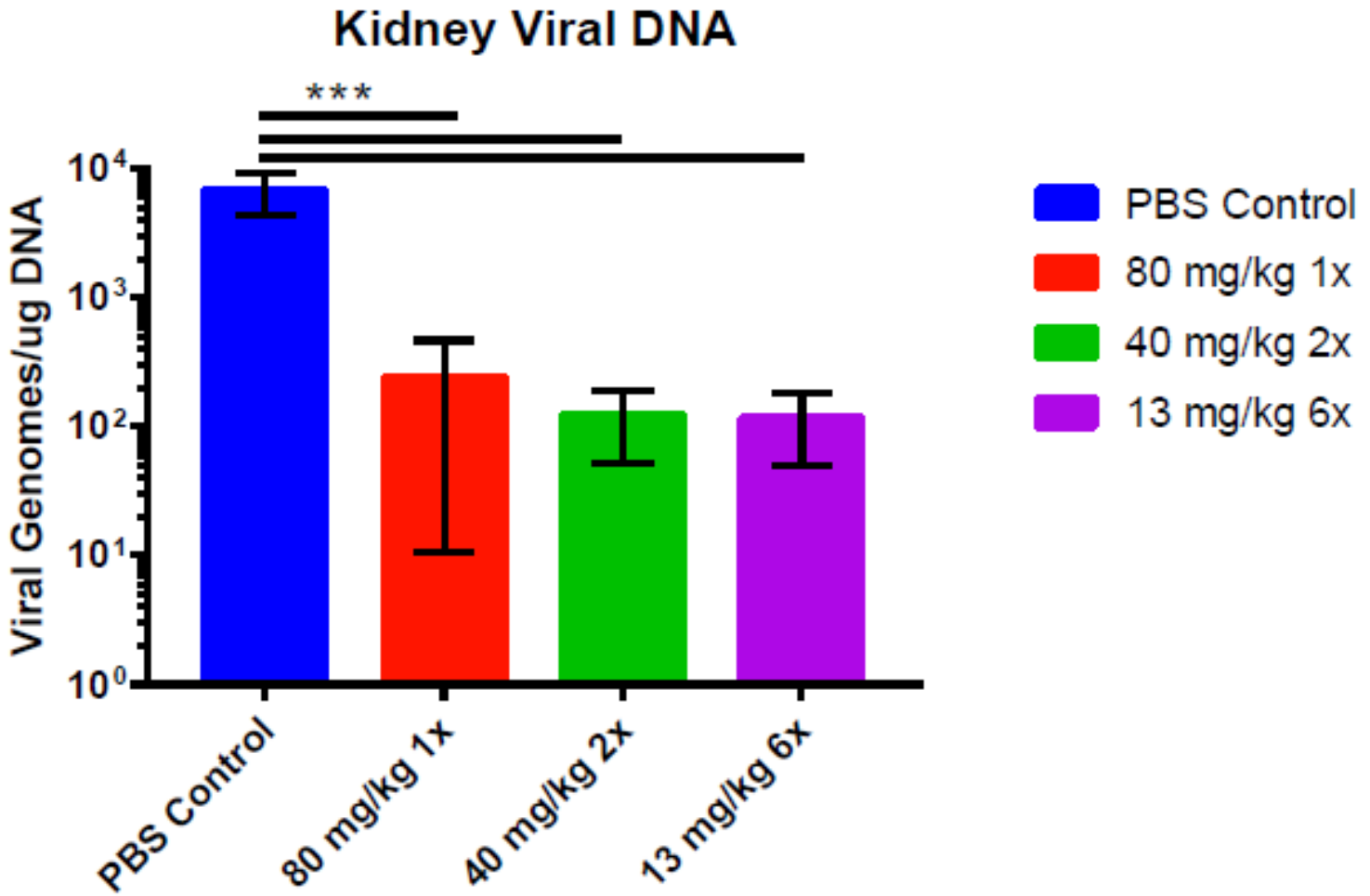
New Animal Model Data: BCV Demonstrated ~2 log_{10} Reduction in Virus in Mouse Kidney after Acute Infection



*Bars represent mean ± SD; Mann-Whitney test- *** p<0.001*

Kidney Week 2018, Abstract SA-PO642

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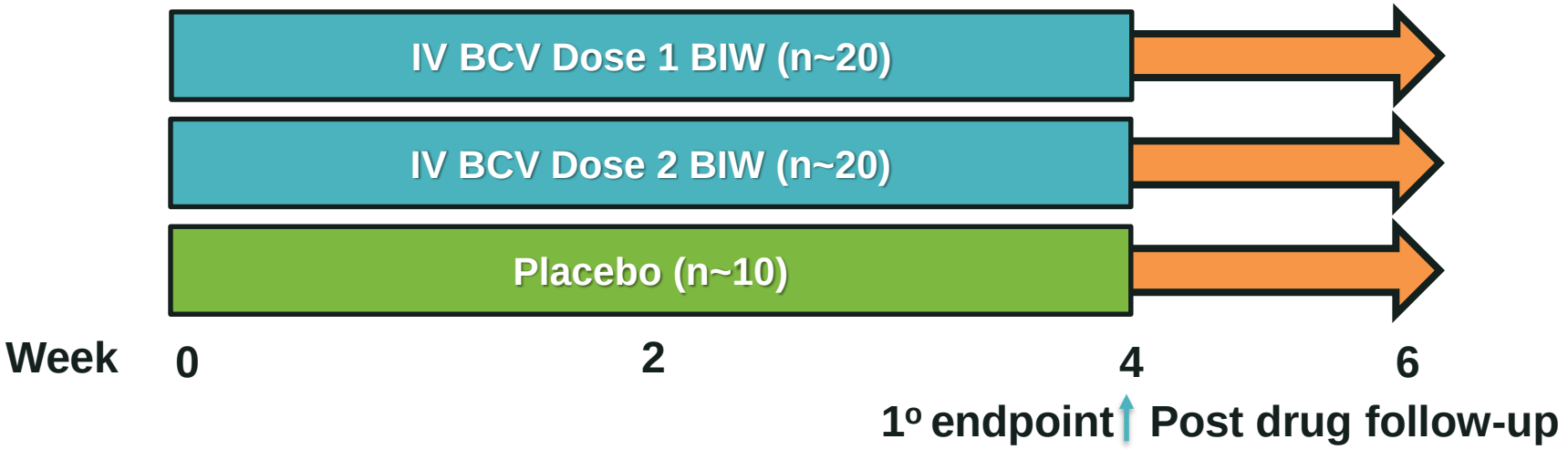
BKV: Potential Proof-of-Concept Study in Kidney Transplant Recipients with BK Viremia

- **Objective: demonstrate antiviral effect of IV BCV on BK Virus (Proof-of-Concept)**
- Population: Kidney transplant with plasma BKV >1,000 c/mL at screen
- Primary endpoint: BK viremia area under the curve minus baseline (AAUCMB) at Wk 4
  - No extension phase - simple, cost effective design for POC



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Brincidofovir: Potent Broad Spectrum Antiviral, Multiple Opportunities for Clinical Development of IV BCV

Viral Family	Virus	BCV	Cidofovir	Maribavir	Letermovir	Ganciclovir*	Foscarnet	Acyclovir
Adenovirus	Adenovirus (AdV)	0.02	1.3	—	>10	4.5-33	Inactive	>100
Polyoma	BK Virus (BKV)	0.13	115	—	—	>200	Inactive	>200
	JC Virus (JCV)	0.045	>0.1	—	—	—	Inactive	—
Papilloma	Human Papillomavirus (HPV)	17	716	—	—	Inactive	—	Inactive
Herpes Viruses	Herpes Simplex Virus 1	0.01	3.0	Inactive	>10	0.7	92-95	3.8
	Herpes Simplex Virus 2	0.02	6.5	Inactive	>10	2.5	91-96	4.4
	Varicella Zoster Virus (VZV, HHV3)	0.0004	0.5	Inactive	>10	1.3	39.8	3.6
	Epstein-Barr Virus (EBV, HHV4)	0.03	65.6	0.63	>10	0.9	<500	6.2
	Cytomegalovirus (CMV, HHV5)	0.001	0.4	0.31	0.005	3.8	50-800	>200
	Human Herpesvirus 6	0.003	2.7	Inactive	>10	5.8	16	10
	Human Herpesvirus 8	0.02	2.6	Inactive	—	8.9	177	>100
Pox	Variola	0.1	27	—	—	—	—	—
	Vaccinia	0.8	46	—	—	>392	Inactive	>144

Potency expressed as EC50 = concentration in μM required to reduce viral replication by 50% in vitro; "—" indicates no data.
*Valganciclovir is rapidly converted to ganciclovir in vivo; ganciclovir is the relevant compound for cell activity studies.
Source: Data are compiled from multiple sources and include multiple materials and methodologies.

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MARKET OPPORTUNITIES FOR BRINCIDOFOVIR

Kevin Reeves
Vice President, Commercial

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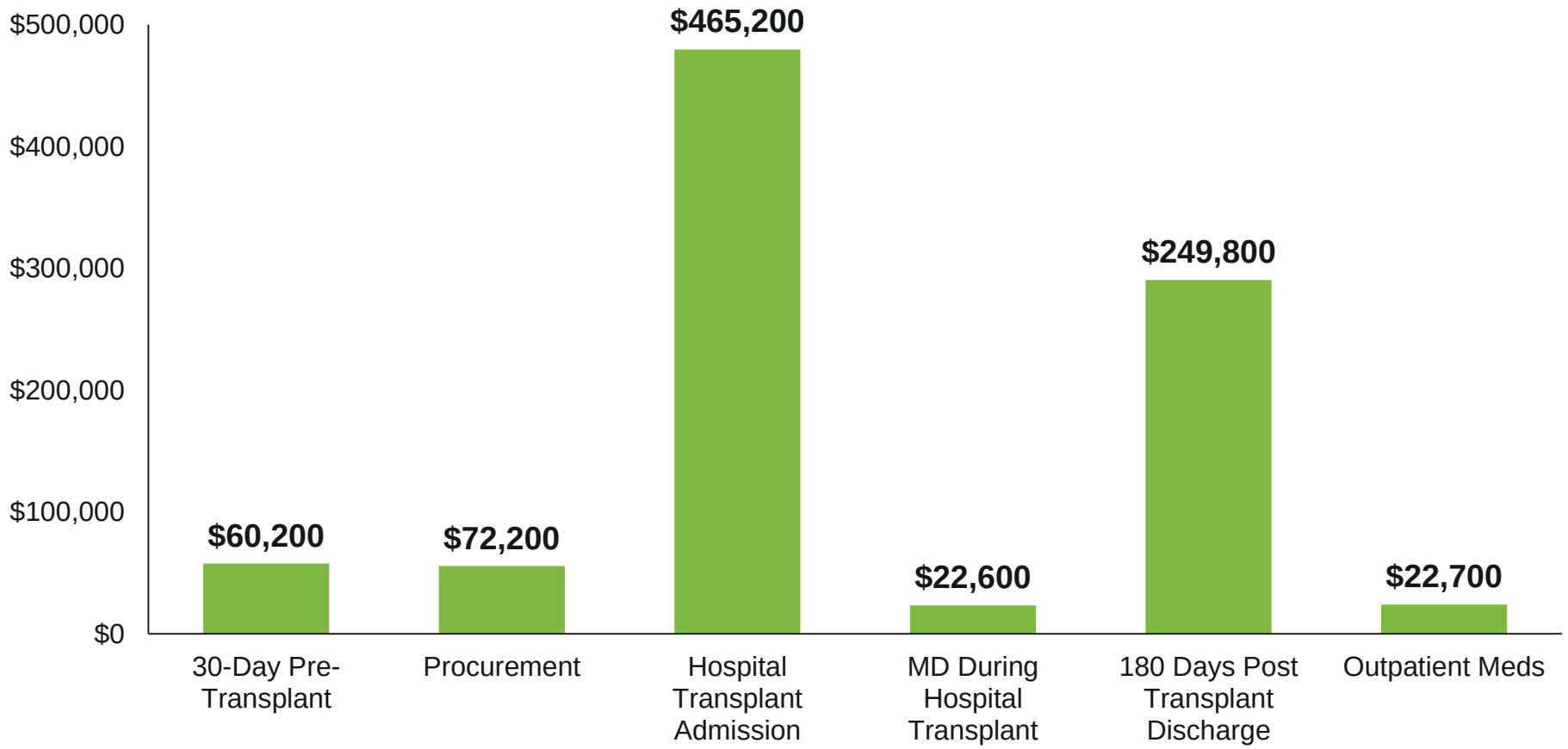
Estimated Average Billed Charges for Allo-HCT in 2017: ~$900,000



Milliman Research Report 2017

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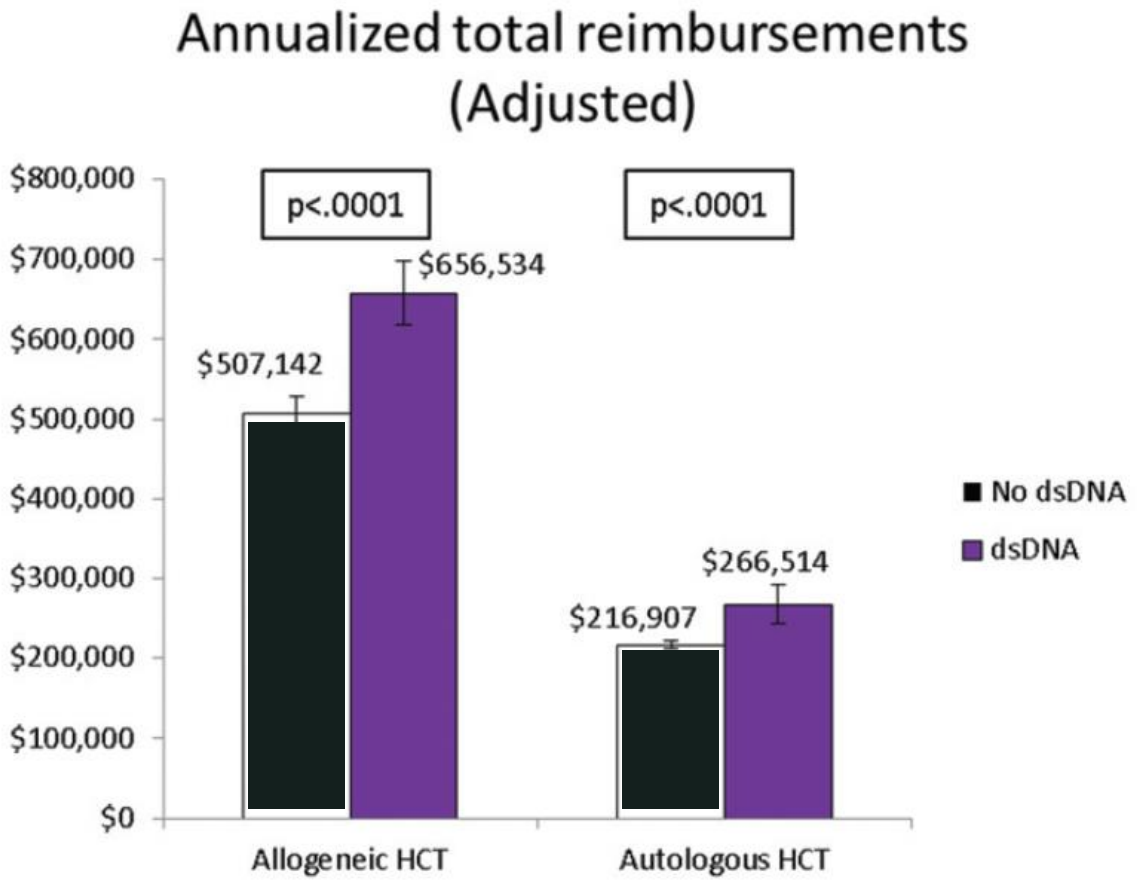
$150,000 Difference between Cost of Allo-HCT with or without dsDNA Viral Infection

- In both allo-HCT and auto-HCT, dsDNA viral infection have a substantial impact on the average reimbursements for the transplant
- Specifically for allo-HCT, ~$150,000 difference for a single dsDNA viral infection in the first year post-HCT



ISPOR EU 2018

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BCV Commercial Considerations

Adenovirus:

- AdV is an orphan indication with no competition
- AdV is a life-threatening condition in pediatric and adult transplant recipients
- HCT recipients have to-date been considered a significant investment by payers

Brincidofovir (BCV):

- First indication is targeting a treatment rather than prophylaxis
  - No patients exposed who will not reactivate virus
- Pricing likely to be based on a course of therapy as determined by AdAPT data

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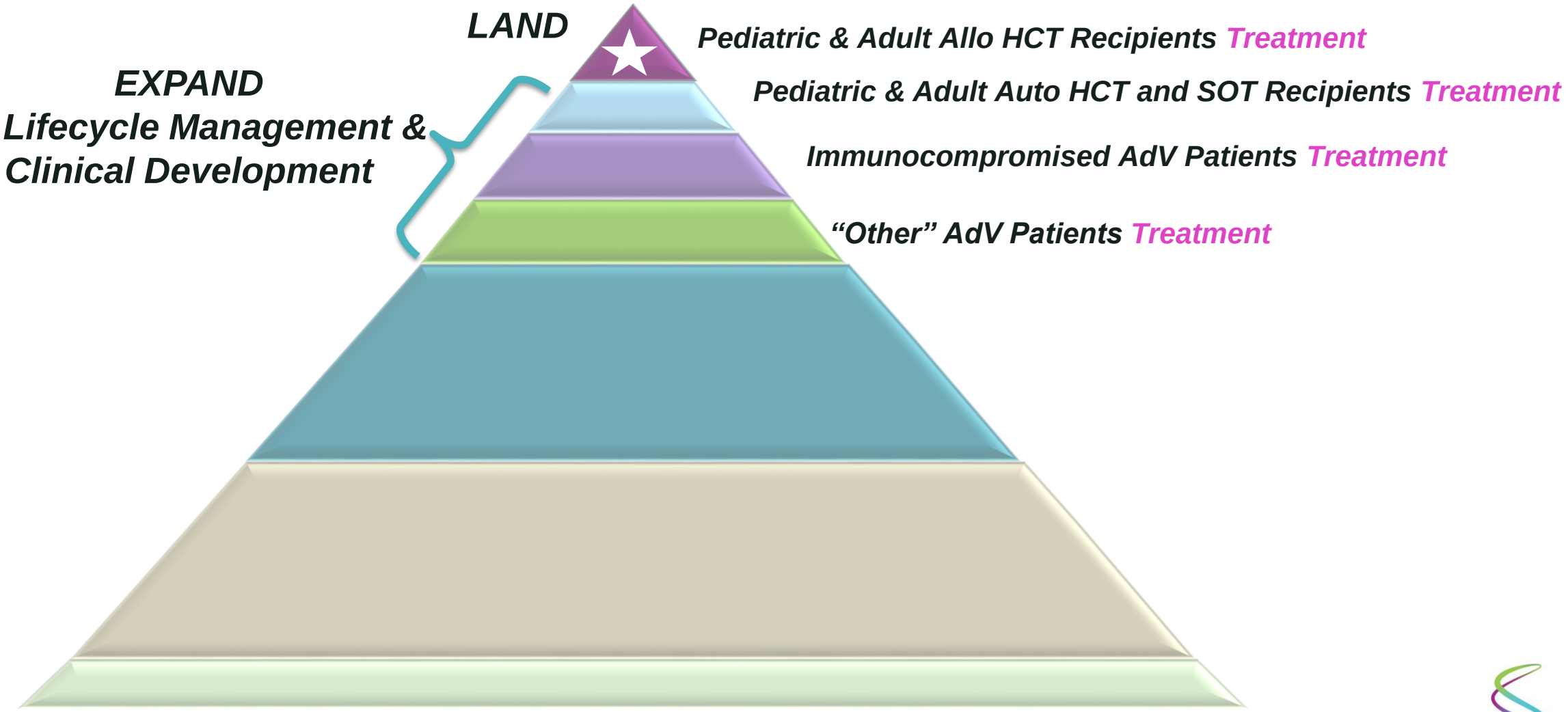
Building Full Potential Value in *Adenovirus:* "Land and Expand"



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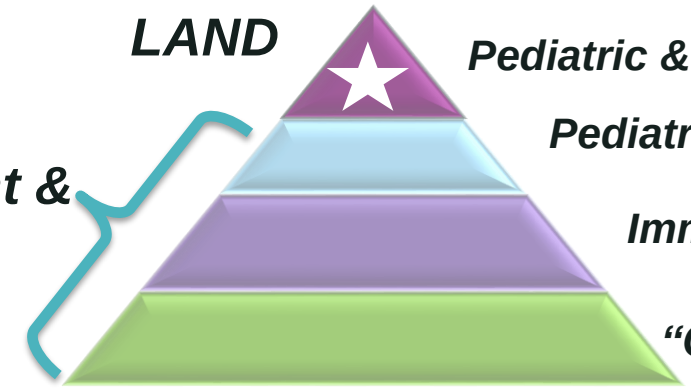
Building Full Potential Value in *Adenovirus:* "Land and Expand"

EXPAND
Via Lifecycle Management & Clinical Development



LAND

Pediatric & Adult Allo HCT Recipients Treatment

Pediatric & Adult Auto HCT and SOT Recipients Treatment

Immunocompromised AdV Patients Treatment

"Other" AdV Patients Treatment

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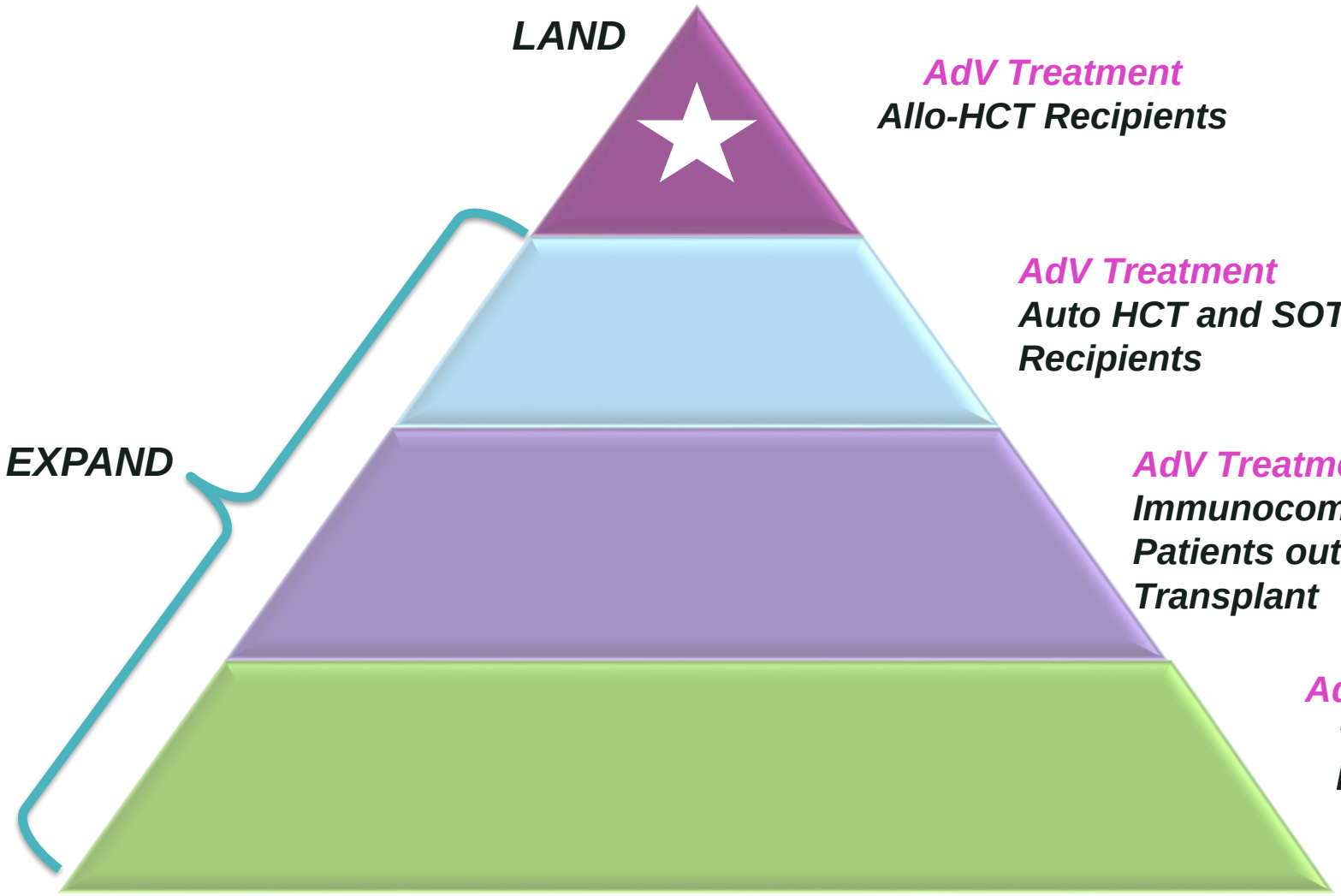
Building Potential Launch Value in AdV through "Land and Expand"



	US and EU Eligible Populations:
AdV Treatment ***Allo-HCT Recipients***	***1,300***
AdV Treatment ***Auto HCT and SOT Recipients***	***2,800***
AdV Treatment ***Immunocompromised Patients outside of Transplant***	***1,800***
AdV Treatment ***"Other" AdV Patients***	***>12,000***
	5,900

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~12,000 Pediatric Hospitalizations for AdV Annually

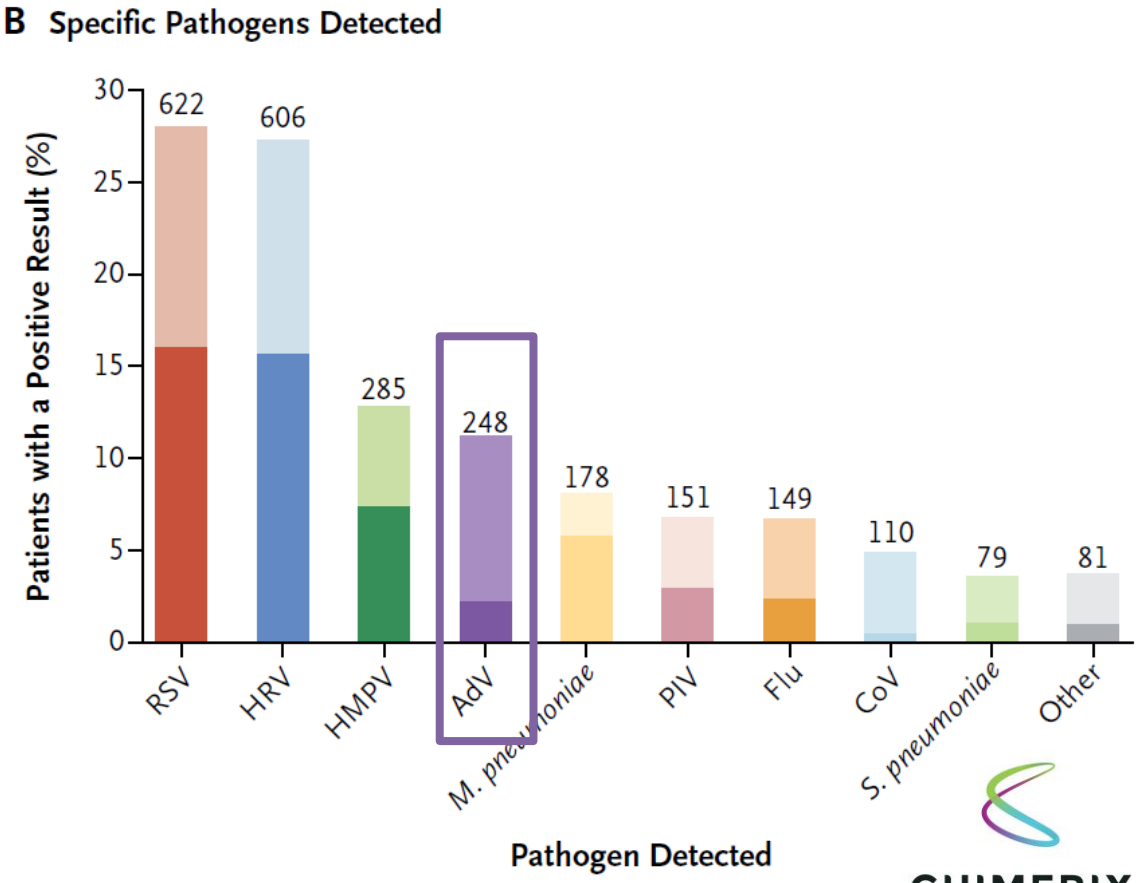
- 2,638 eligible children enrolled
  - 51% had underlying condition (asthma 33%, preterm 21%)
  - 21% required intensive care, and 3 (<1%) died
- Pneumonia: 15.7 cases per 10,000 children
- **Adenovirus was detected in 11%**
  - More common among younger children <5 yo (15%) vs. ≥ 5 yo (3%)
- **Hospitalized AdV pneumonia occurs in 1.6 per 10,000 kids in US annually:**
  - **~12,000 cases per year**

N Engl J Med 2015; 372: 835-45. DOI: 10.1056/NEJMoa1405870

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Community-Acquired Pneumonia Requiring Hospitalization among U.S. Children



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Global Opportunities in Stem Cell and Solid Organ Transplant



TRANSPLANTS PER YEAR	US	EU 28-40	Japan	Total
HCT				
Allogeneic	8,700	16,200	3,700	28,600
Autologous	15,100	24,800	1,800	41,700
HCT TOTALS	23,800	41,000	5,500	70,300
SOT				
Kidney	20,600	21,100	1,648	43,348
Liver	8,100	8,000	438	16,538
Other SOT	6,000	4,900	124	11,024
SOT TOTALS	34,700	34,000	2,210	70,910
TOTAL TRANSPLANT	58,500	75,000	7,710	141,210

US HCT: 2015 figures from CIBMTR. Auto-HCT are increased by 20% to account for under-reporting to CIBMTR. US SOT: 2017 figures from Organ Procurement and Transplantation Network (OPTN)
EU HCT: JR Passweg, et al., 2016 EBMT Transplant Activity Survey (includes 40 EU countries; non EU countries removed). EU SOT: EDQM's Newsletter Transplant – Internat'l Figures on Donation & Transplantation 2017 (includes 28 EU countries).
Japan: Clarivate Japan assessment (HCT for 2015; Kidney/Liver for 2016; Other SOT for 2015)

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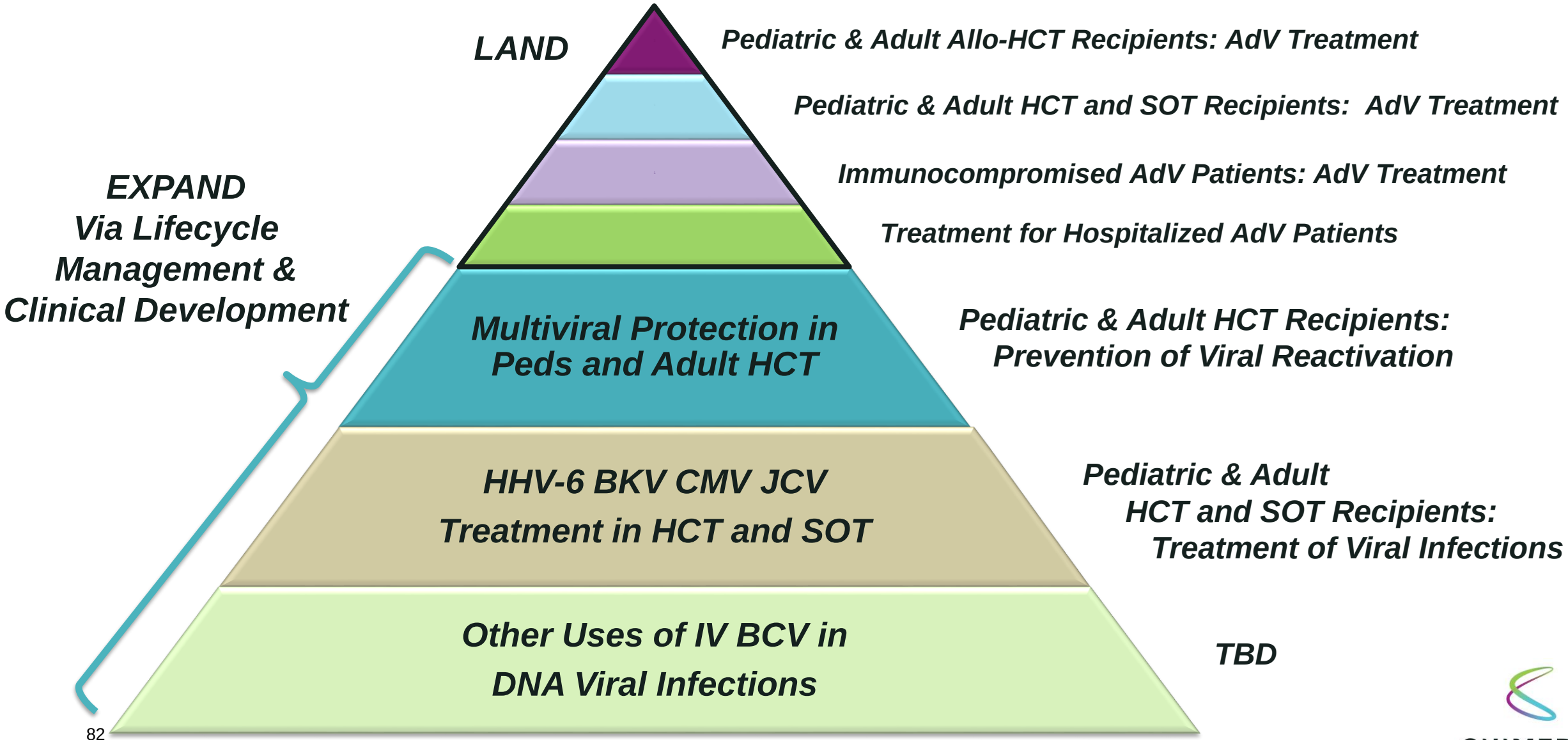
Building Potential Value for Oral and IV BCV: "Land and Expand"



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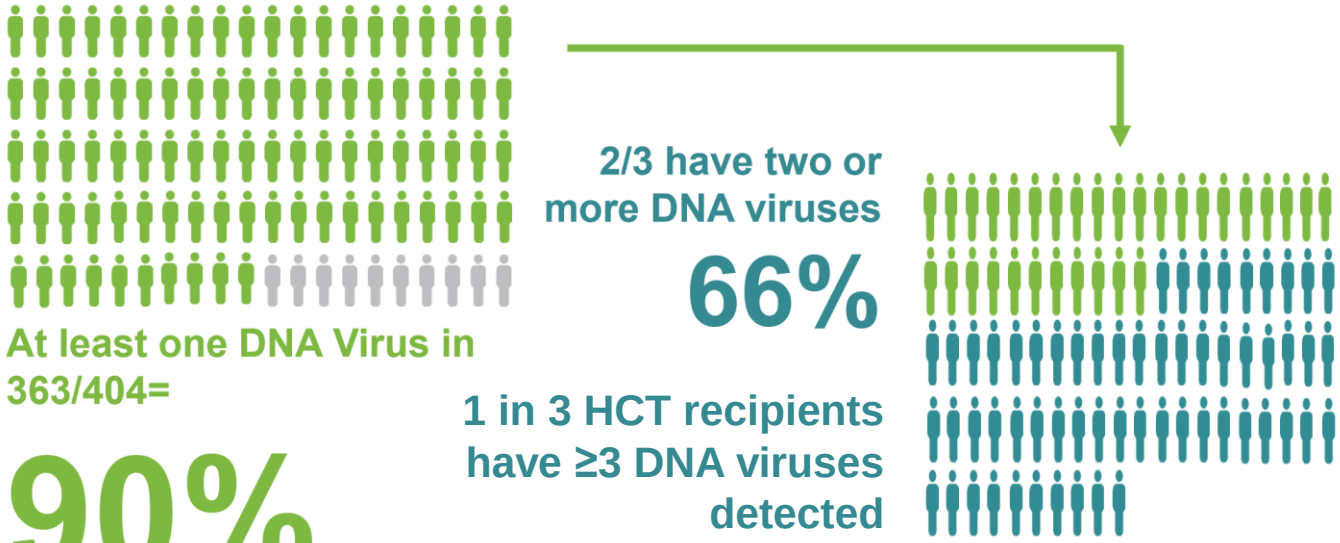
Allo-HCT Patients Are at Risk of Multiple DNA Virus Infections

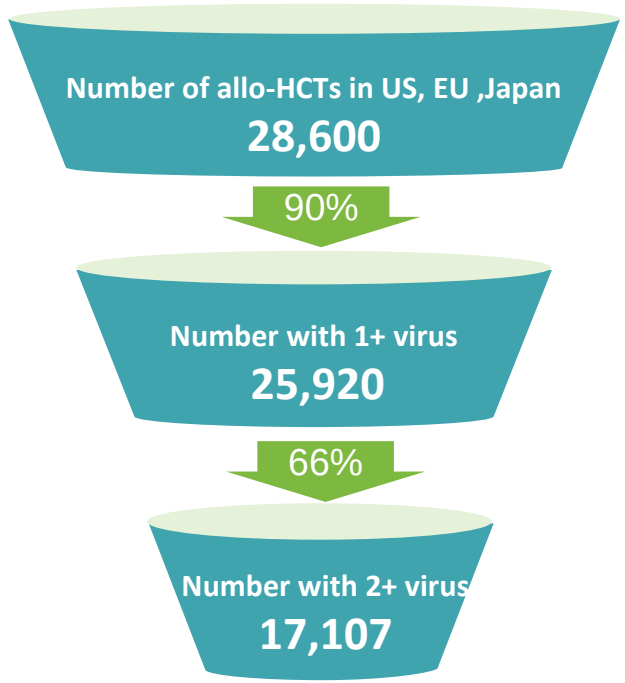
Number of patients with reactivation of viruses after HCT*



Reactivation of multiple viruses is very common in HCT patients

*Hill J et al. Blood. 2017 Feb 16

Considerations for Clinicians



Multi-viral protection is needed in these patients

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Potential for IV BCV in Other DNA Virus Infections: BK Virus

- Both SOT and HCT recipients are at risk for BKV infections
  - HCT: hemorrhagic cystitis requiring hospitalization for pain control
  - Kidney transplant recipients: BKV associated nephropathy with risk of graft loss and a return to dialysis or wait-list for re-transplant
- No approved therapy for treatment or prevention
- Reported incidence:
  - 16% of Allo-HCT recipients develop BKV hemorrhagic cystitis
  - Up to 10% of kidney transplant recipients develop BKV viremia in the first year post-transplant

BK Patient Potential HCT	BK Patient Potential SOT
~4,600	~5,300

Epi rates: Hirsch et al. Am J Transplantation 2013; Rorije et al. ASBMT 2014;

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CMRX: Advancing BCV Toward High Value Opportunities

Program	Indication	Pre-clinical	Phase 1	Phase 2	Phase 3	Est'd patients in U.S. and EU
Short-course Oral BCV	AdV Treatment					~ 5,900
	Smallpox					1.7M course Procurement*
IV BCV	AdV					~ 5,900
	BK virus	*Dose-Ranging Planned*				~9,900
	Multi-viral	*Planned*				~17,000
	HHV-6					TBD

*Based on previous 2015 RFP request

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CMX521 FOR NOROVIRUS

Randall Lanier, PhD
Chief Scientific Officer

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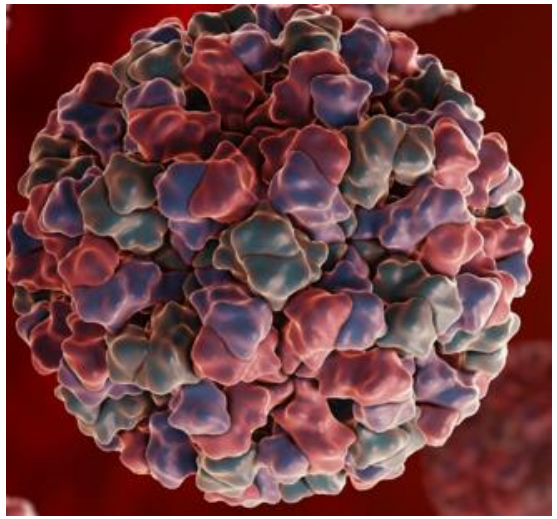
Human Norovirus Infections Are Prevalent and Costly

- Worldwide: ~700 million cases of norovirus each year (~20 million in U.S.)
  - ~219,000 deaths per year[1]
  - 15-20 percent of HCT and SOT patients get NV in first year
    - associated with chronic, severe diarrhea and graft rejection



- Economic toll of norovirus is >$60 Billion per year[2]
  - $4.2B in direct health system costs; ≈56B in productivity losses
  - >60% of outbreaks in US occur in long-term care facilities

- Nothing approved for prevention or treatment
  - Norovirus genetic diversity is a significant hurdle for antivirals and vaccines
  - Ideal therapy should work against all strains

1 PLoS Med 13(4):e1001999
2 PLoS ONE 11(4):e0151219

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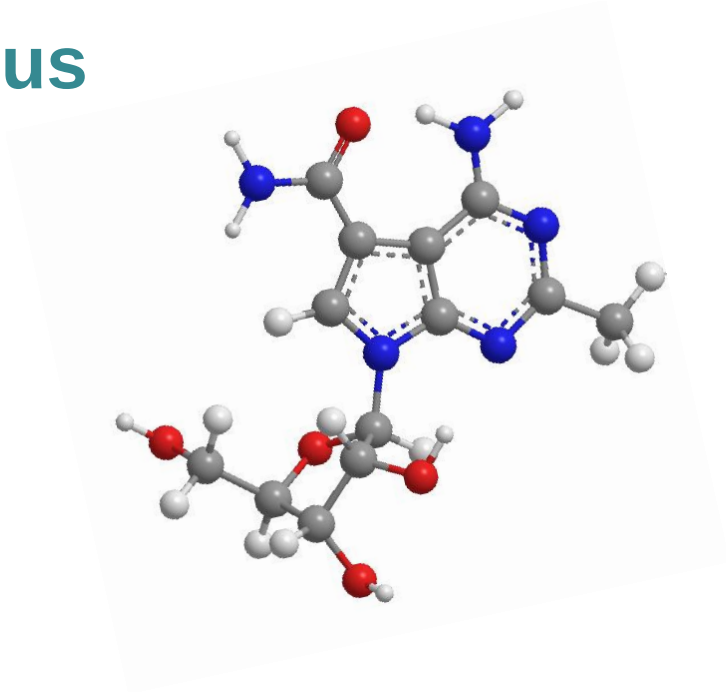
CMX521: A Small Molecule Antiviral for Norovirus



- Nucleoside with pan-genotype activity
  - Targets region of virus that is common to all strains
- Safety profile looks very promising
  - Phase 1 data showed single doses were safe and well-tolerated
- Patent protection until 2036

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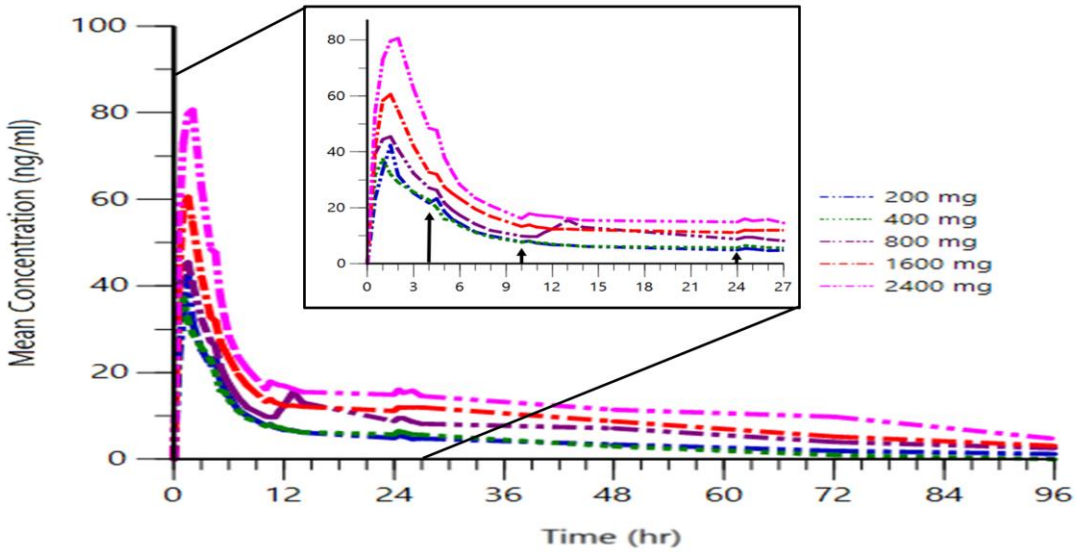
CMX521 Update: Single Ascending Dose Study

Cohort	N	Single Dose of CMX521 or Placebo
1	4 active/2 placebo	200 mg
2	6 active/2 placebo	400 mg
3	6 active/2 placebo	800 mg
4	6 active/2 placebo	1600 mg
5	6 active/2 placebo	2400 mg

PK: Mean Plasma CMX521 Concentration vs Time After Single Oral Dose (All Subjects)



- CMX521 plasma exposures increased in a less-than-proportional manner with escalating single oral dose administration
- Single oral doses of CMX521 up to 2400 mg were generally well-tolerated. No safety concerns were identified
- These data support continuing the development of CMX521 for human norovirus infections

European Society of Clinical Virology 2018 poster 270

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Discovery Virology Goal:

"Deliver effective concentrations of the active antiviral to the right place without causing toxicity"

Activity in vitro

Target cells in vivo
Optimize benefit/Minimize risk

Effective/Well-tolerated dose in people

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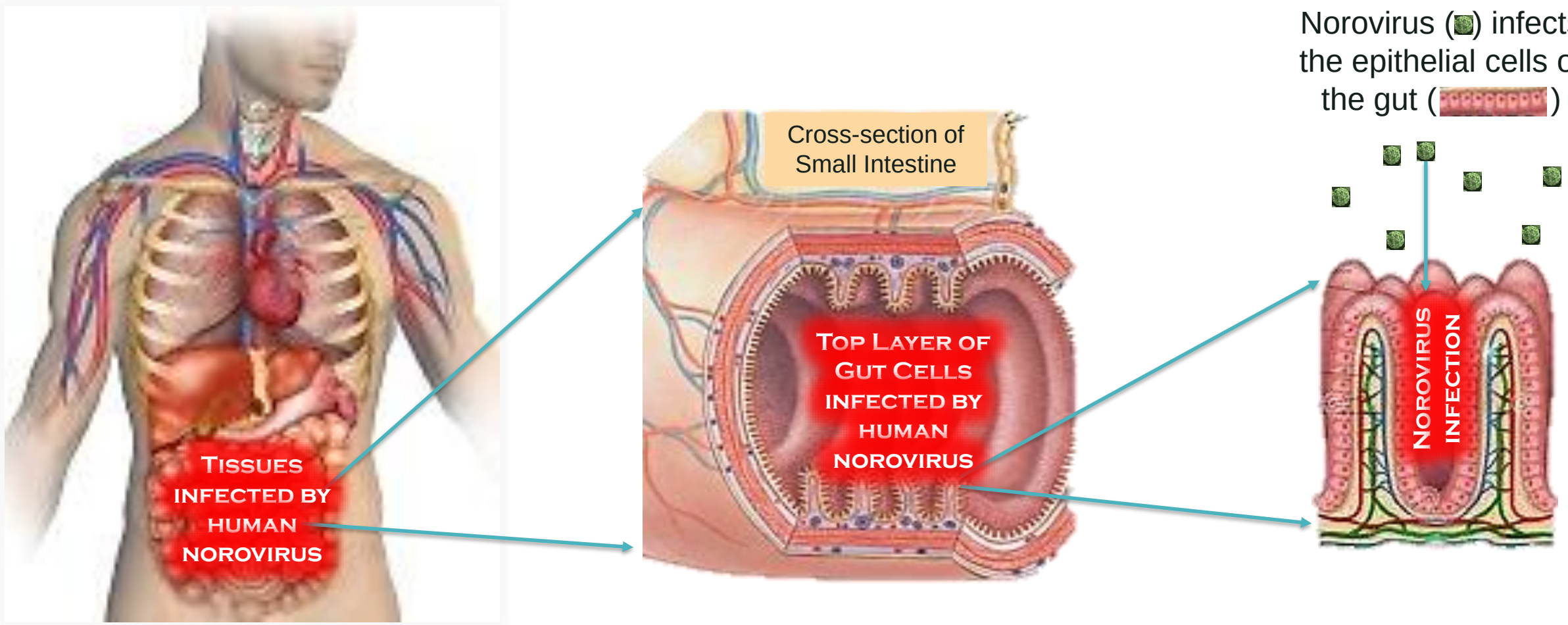
Norovirus Infects Cells Lining the Gut in Humans



- Human norovirus replicates in “enterocytes” lining the gut
- Primary target cells for a norovirus therapeutic in the gut epithelia

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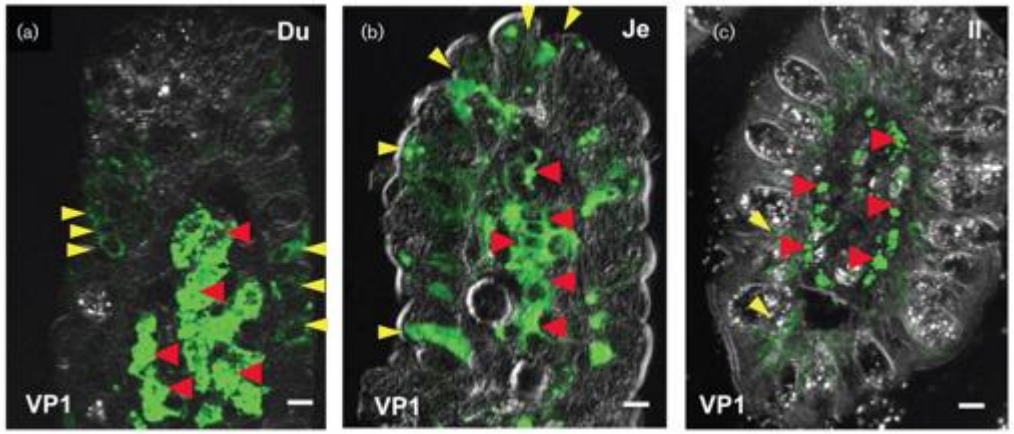
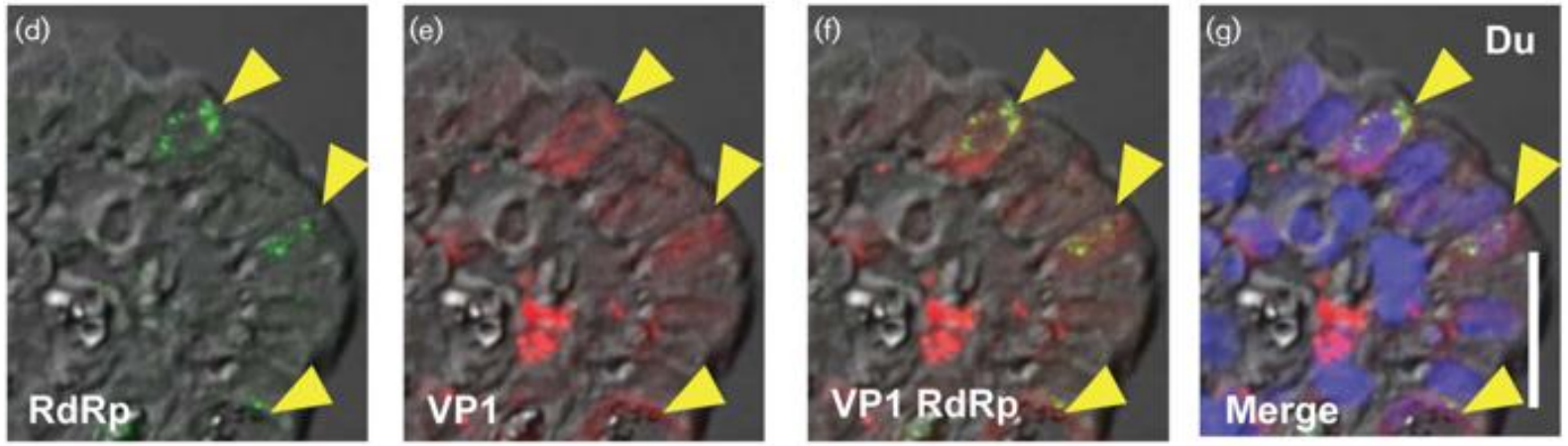
Human Norovirus Replicates in Enterocytes Lining the Gut



Detection of NV in the duodenum (a), jejunum (b) and ileum (c). Infection in enterocytes (yellow arrows) and GALT of lamina propria (red arrows).



Colocalization of RdRp and VP1, indicating replication in enterocytes.

Karandikar et al. 2016 (97)

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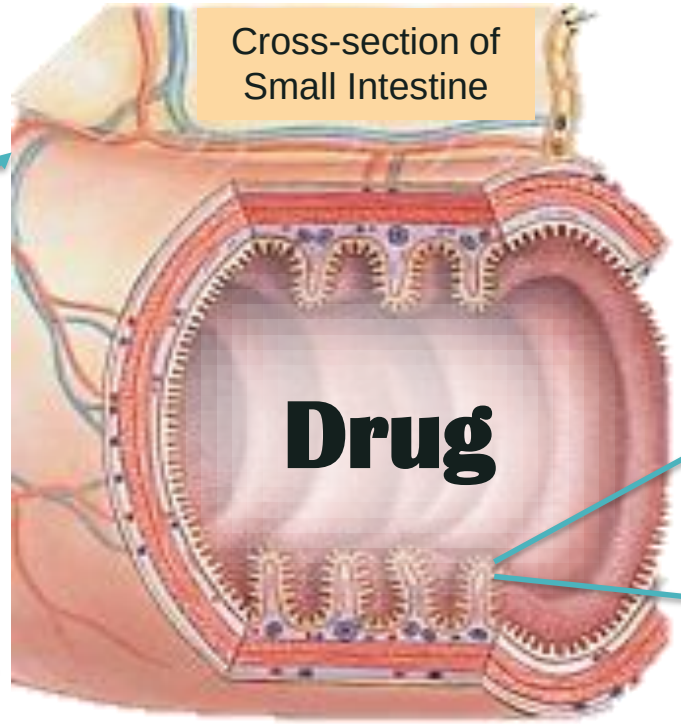
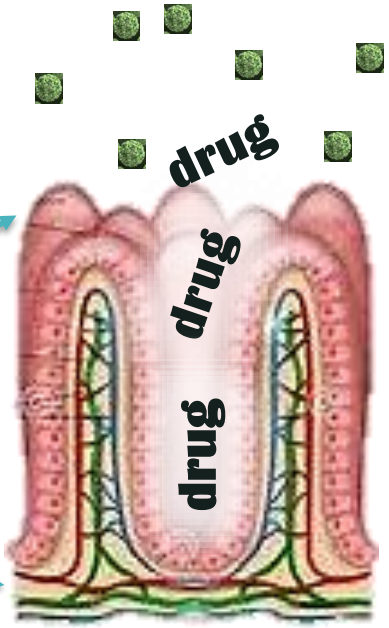
Drug Preferentially Delivered to Target Cells with Oral Dosing



Norovirus ( ) infects the epithelial cells of the gut ( )



- More drug in target sites improves efficacy
- Less drug in non-target sites improves safety

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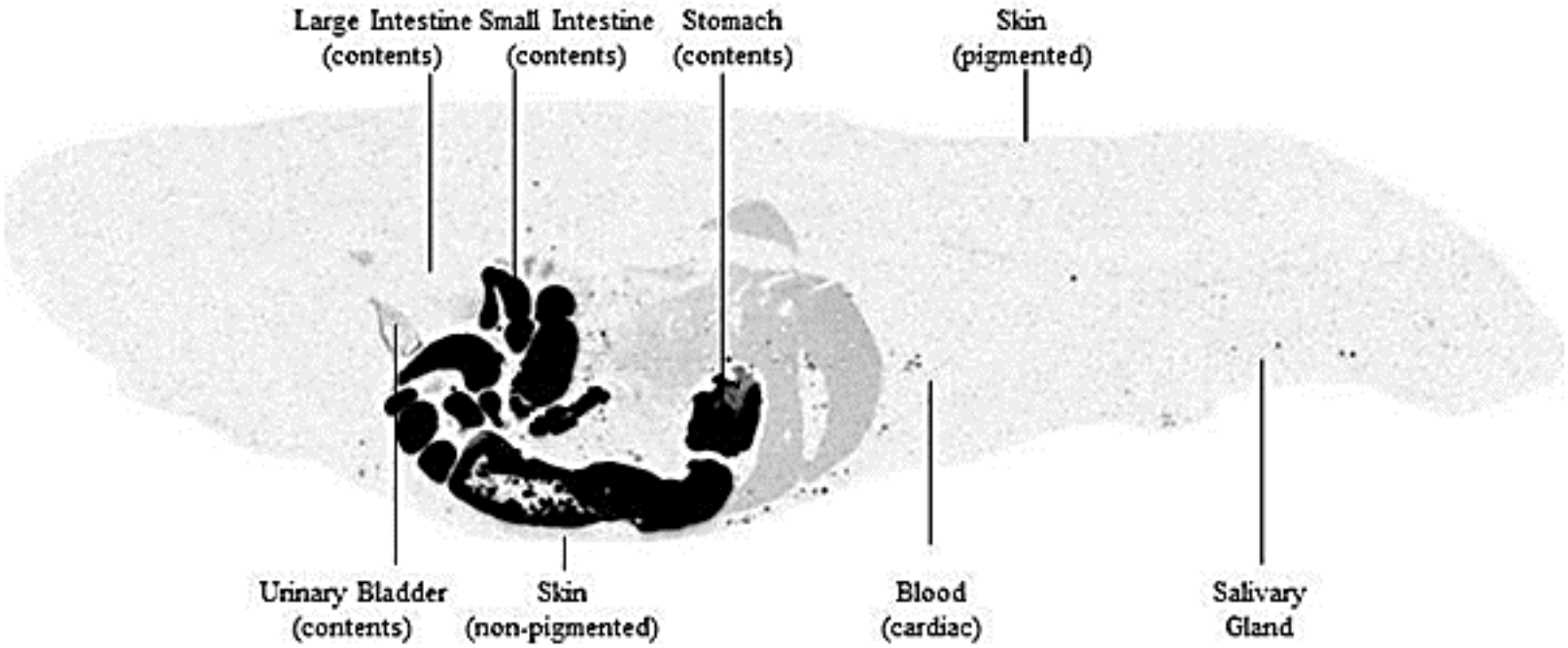
Oral CMX521 Preferentially Delivered Drug to Gut in Rats



4 hours after Oral administration of 50 mg/kg [^{14}C]CMX521

Radioactive drug preferentially contained in intestines after oral dosing

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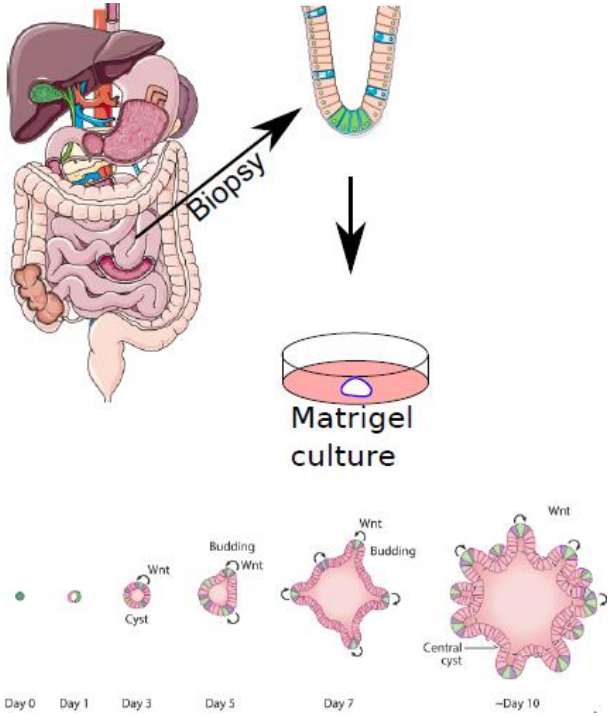
Opportunity to Find an “Effective” Dose in Phase 1 and De-Risk Later Stage Clinical Development



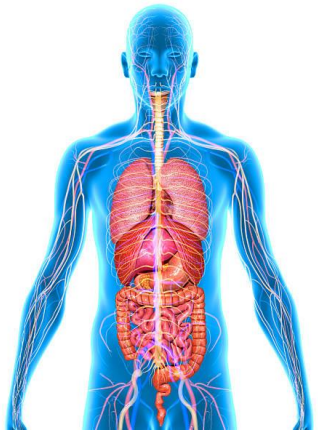
[Active drug] in cultured human enterocytes at the EC50/90/99

[active drug]

[active drug]

[active drug]

[Active drug] that prevents norovirus disease in mice



[Active drug] in humans at well-tolerated doses

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Two Promising Scenarios for Norovirus Antivirals

- **Treatment** of **Chronic** Norovirus Infection
  - Transplant recipients and other symptomatic immunocompromised patients
  - Asymptomatic shedders
    - Food handlers, hospital/healthcare workers who may be source of outbreaks

- **Prevention** of **Acute** Norovirus Infection
  - Protect individuals from a potential outbreak (hospitals, long-term care facilities etc.)
  - Significantly reduce the economic impact of outbreaks

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CMRX: A Robust Pipeline for High Value Opportunities

Program	Indication	Pre-clinical	Phase 1	Phase 2	Phase 3	Est'd Market Opportunity
Short-course Oral BCV	AdV Treatment					~ 5,900
	Smallpox					1.7m courses Procurement*
IV BCV	AdV					~ 5,900
	BK virus	*Dose-Ranging Planned*				~9,900
	Multi-viral	*Planned*				17,000
	HHV-6					TBD
CMX521	Norovirus					~700 MM cases of norovirus each year worldwide

- Chimerix remains well-capitalized with $196M at the end of 2Q2018
- Patent protection into 2034 for brincidofovir, and 2036 for CMX521

*Based upon previous 2015 RFP request

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