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INVESTOR UPDATE

APRIL 27, 2017

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. 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 Annual Report on Form 10-K for the year ended December 31, 2016 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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Agenda

- Prof. Thomas Lion
  - AdV epidemiology and pathophysiology of childhood AdV
  - Pathophysiology of AdV infections in pediatric patients and the role of stool monitoring
- Dr. Garrett Nichols
  - AdAPT (**A**denovirus after **A**llogeneic **P**ediatric **T**ransplant) study plans, timing and probability of success
- Dr. Josh Hill
  - Frequency and associated outcomes of DNA viral reactivation
- Dr. Garrett Nichols
  - IV BCV data from SAD, plans for MAD and patient-based studies to support pivotal study MVP-Peds for **M**ulti-**V**iral **P**revention in pediatric HCT
- Linda Richardson
  - Market opportunity for serious adenovirus infections and prevention of DNA viral infections in high-risk transplant recipients

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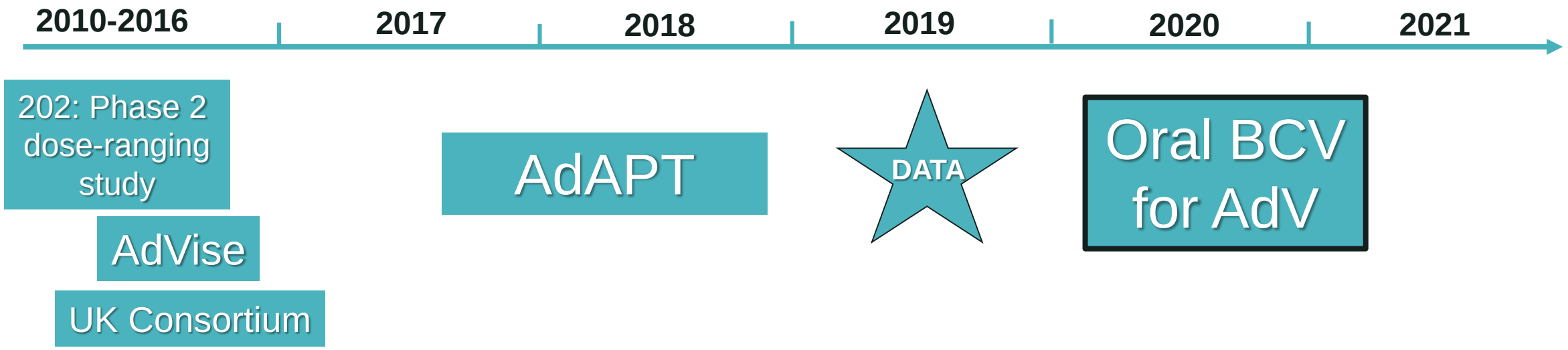
Oral Brincidofovir for Treatment of AdV: Development and Approval Timelines



- AdAPT has been designed together with European regulators to provide a small randomized study of oral BCV for short-course treatment of AdV
- AdAPT should provide data sufficient for a conditional or full approval

All timelines are estimated

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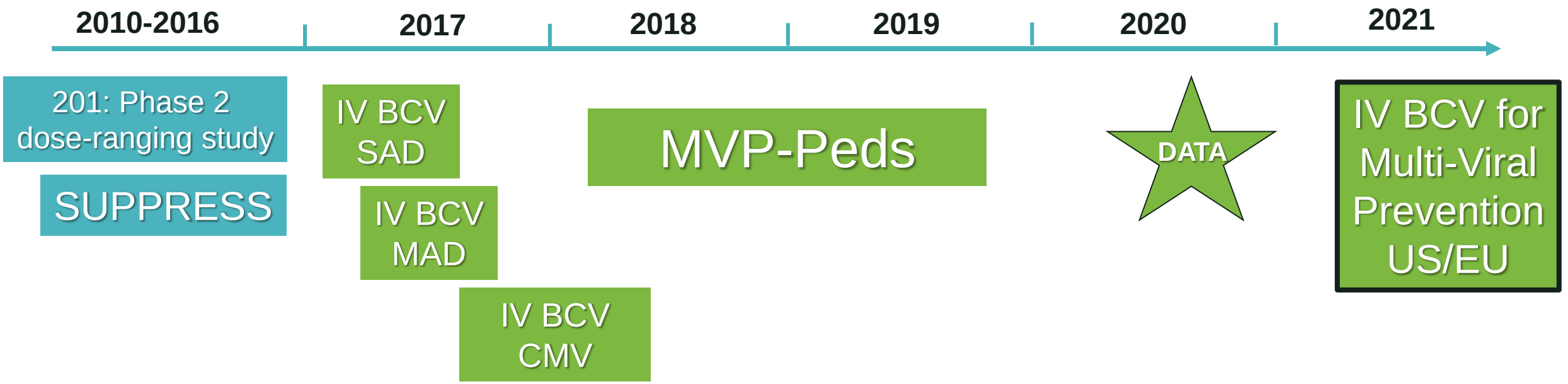
IV Brincidofovir for Multi-Viral Prevention in HCT Recipients: Development and Approval Timelines



- MVP-Peds provides the opportunity to demonstrate the importance of preventing multiple DNA viral infections in a placebo-controlled superiority pivotal study

All timelines are estimated

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Chimerix Pipeline

	Program	Discovery	Pre-clinical	Phase 1	Phase 2	Phase 3	Anticipated Approval
Short-course Oral BCV	AdV Treatment	AdAPT in EU (+/- US) to start in 2H 2017					2020
	Smallpox	Data from second animal efficacy model in 2017					2019
IV BCV	Multi-viral Prevention	Data from MAD in 2017			Ph 2/3 MVP-Peds HCT		2021
	CMV Treatment	Initiate Dosing late 2017					
	BKV Treatment	Initiate Dosing 2018			Ph 2/3 in Kidney Tx		2023
CMX521	Norovirus	IND 2H 2017		FTIH & POC	Prevention Field Testing & Treatment Ph 3		2022
CMX157	HBV Treatment	*Licensed to ContraVir					

All timelines are estimated
* Development per ContraVir's website

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EPIDEMIOLOGY, BIOLOGY, AND DIAGNOSIS OF ADENOVIRUS INFECTIONS AFTER HCT

Prof. Thomas Lion, MD, PhD
CCRI/ LabDia Labordiagnostik GmbH
Thomas.Lion@CCRI.at

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Adenoviruses

- **Non-enveloped double-stranded DNA viruses**
- **7 Species (A-G), 80+ types**
- **Diverse organ tropism/affinity**

AdV Species and Organ Tropism

A	Intestine; CNS
B	Respiratory tract; Eye; Intestine; Genitourinary tract; CNS
C	Respiratory tract; Intestine; Liver
D	Eye; Intestine; CNS
E	Respiratory tract; Eye
F, G	Intestine

Clinical Manifestations

Gastroenteritis

Pneumonia

Hemorrhagic cystitis

Meningoencephalitis

Hepatitis

Kerato-conjunctivitis

Respiratory infection

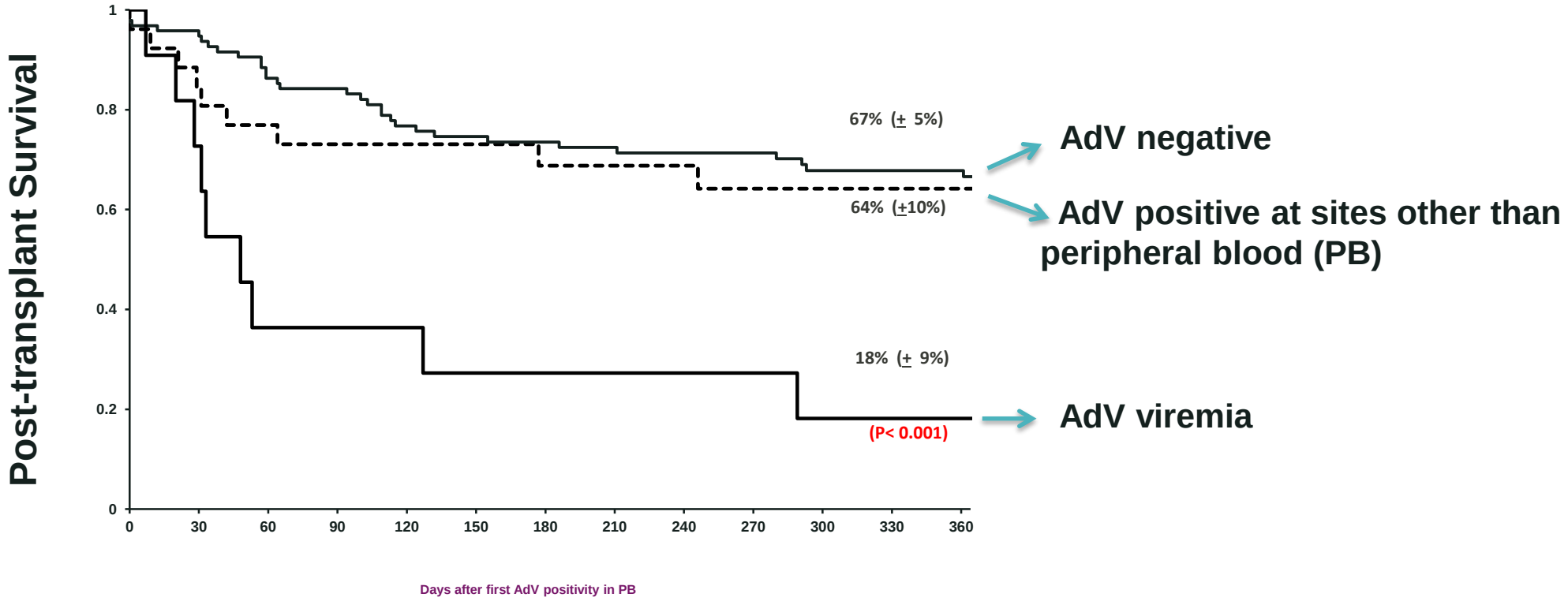
AdV in Immune Competent vs Immunosuppressed Patients

- Generally self-limited and mild courses
- Occasional outbreaks with high infectivity and fatal outcomes
  - Severe lung infections[1-3] reported in military barracks, measles-related pneumonitis
  - Myocarditis[4]
- Patients with underlying respiratory disease[5] (asthma, COPD, cystic fibrosis)

- Post-HCT infection/reactivation with high rates of mortality[6]
- Post-SOT (liver) infection/reactivation with fatal courses[7]

1. Hai IT. Emerg Infect Dis. 2016 ; 2. Clemmons NS. Emerg Infect Dis. 2017; 3. Zhang SY. Infect Dis 2016; 4. Savon C J Clin Virol. 2008; 5. Kokturk N. Mol Med Rep. 2015; 6. Lion T. Clin Microbiol Rev. 2014 ; 7. Schaberg KB. Am J Surg Pathol .2017

Adenovirus Detected in Peripheral Blood Is Associated With High Transplant-Related Mortality



AdV positivity in Peripheral Blood ⟺ Transplant Related Mortality (p<0.001)

Lion et al. Blood 2003; Hiwarkar et al. Bone Marrow Transplant 2013

Adenoviremia In Adults Is Less Common But Equally Dangerous

Adults: AdV occurrence (and/or surveillance) less common[1,2]

Year	Author	Adults	Children
		Viremia (lethal)	Viremia (lethal)
2015	Feghoul et al		25% (7/18)
2013	Hiwarkar et al		15% (n.r.)
2012	Sive et al	12% (1/14)	
2012	Taniguchi et al	9% (4/10)	
2012	Watson et al		16% (2/7)
2011	Öhrmalm et al	3% (0/2)	15% (0/3)
2010	Lion et al		10% (8/16)
2009	de Pagter et al		31% (3/19)
2008	Gustafson et al	15% (2/4)	15% (1/2)
2007	Sivaprakasam et al		11% (3/8)
2007	Kalpoe et al	5% (1/5)	14% (3/8)
2006	Yusuf et al		21% (1/37)
2005	van Tol et al		6% (7/21)
2005	Walls et al		42% (2/7)
2004	Avivi et al	14% (3/3)	
2002	Chakrabarti et al	3% (2/2)	

[1]Bruno B, et al. BBMT 2003;9:341-352;
[2]Howard DS, et al. CID. 1999;29:1494-1501

Risk Factors in Allo-HCT for AdV Viremia & Disseminated Disease

- Allo-HCT with unrelated donor or cord blood graft
- Allo-HCT with T-cell depletion
- Severe Graft-vs-host-disease (GvHD) (grade III-IV)
- Severe lymphopenia (<300 CD3+ cells/µl PB)
- Treatment with alemtuzumab (anti CD52 antibody against T- and B- lymphocytes)

Reduction of immunosuppresion, if possible

➡ **Adequate immune response is important for controlling adenoviral infections**

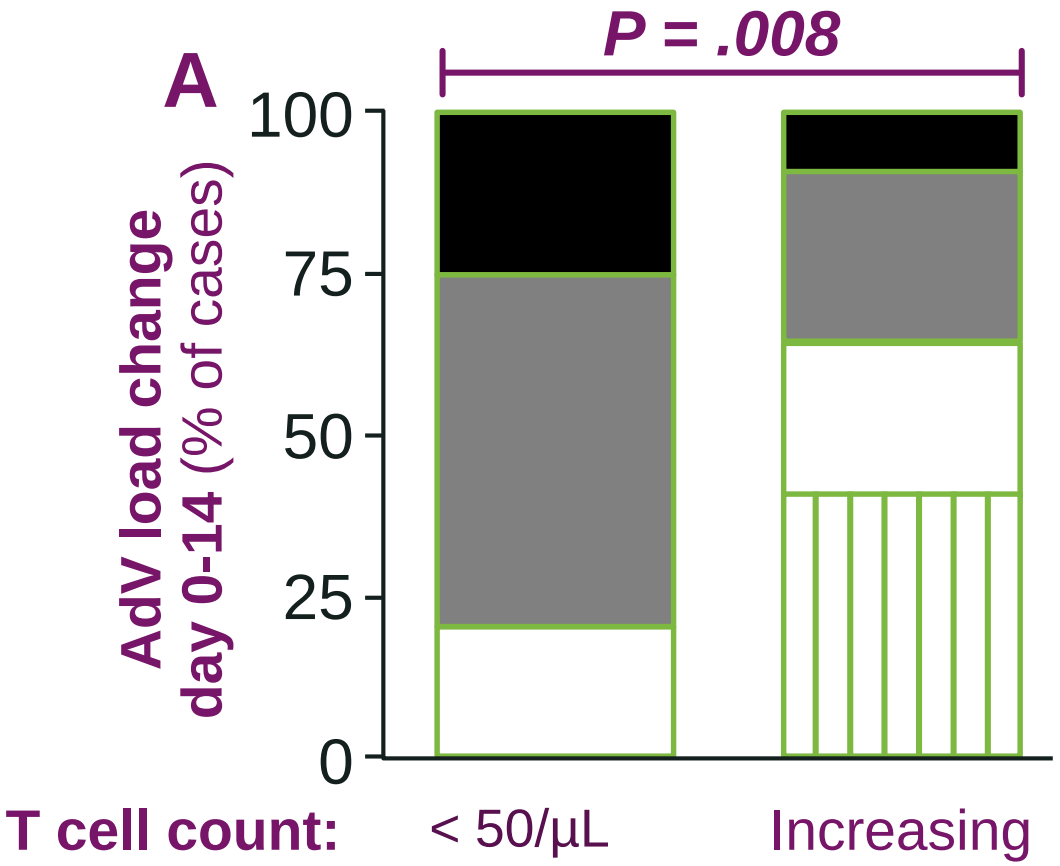
Available Antivirals Provide Limited Utility in AdV Infections

Cidofovir 

currently primary anti-AdV agent (off label) for pre-emptive therapy

activity against all AdV species may allow time for T-cell recovery

Virological Responses to IV Cidofovir Are Dependent on Immune Reconstitution



Increase (≥ 1 log ↑)

Stabilization (< 1 log ↑ / ↓)

Reduction (≥ 1 log ↓)

AdV clearance

Responses to IV CDV when T cells < 50/µL:

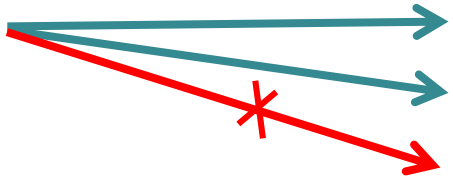
- **increasing AdV viral load (25%)**
- **merely stabilized AdV viral load (>50%)**

Upon improving immune-reconstitution:

- **AdV reduction or clearance (>50%)**

Lugthart *et al*, 2015

Available Antivirals Provide Limited Utility in AdV Infections

Cidofovir 

currently primary anti-AdV agent (off label) for pre-emptive therapy

activity against all AdV species may allow time for T-cell recovery

high risk of nephrotoxicity → *ECIL-4*, Matthes-Martin S. TID 2012*

(Lindemans CA. Blood 2010,116:5476; Neophytos D. BBMT 2007, 13:74-81; Ljungman P. BMT 2003, 31:481-6)

Ribavirin 

documented *in vitro* activity against AdV-C only

questionable therapeutic effect in vivo > added value against AdV-C?

(Morfin F. Antivir Ther 2009, 14:55-61; Lankester A. CID 2004, 38:1521-5) ;Abe S. BMT 2003, 32:1107-8

Ganciclovir 

modest activity due to inefficient phosphorylation (lack of TK in AdV)

(Naesens L. Antimicrob Agent Ther 2005, 49:1010-16; Bruno BT. BMT 2003, 9:341-2)

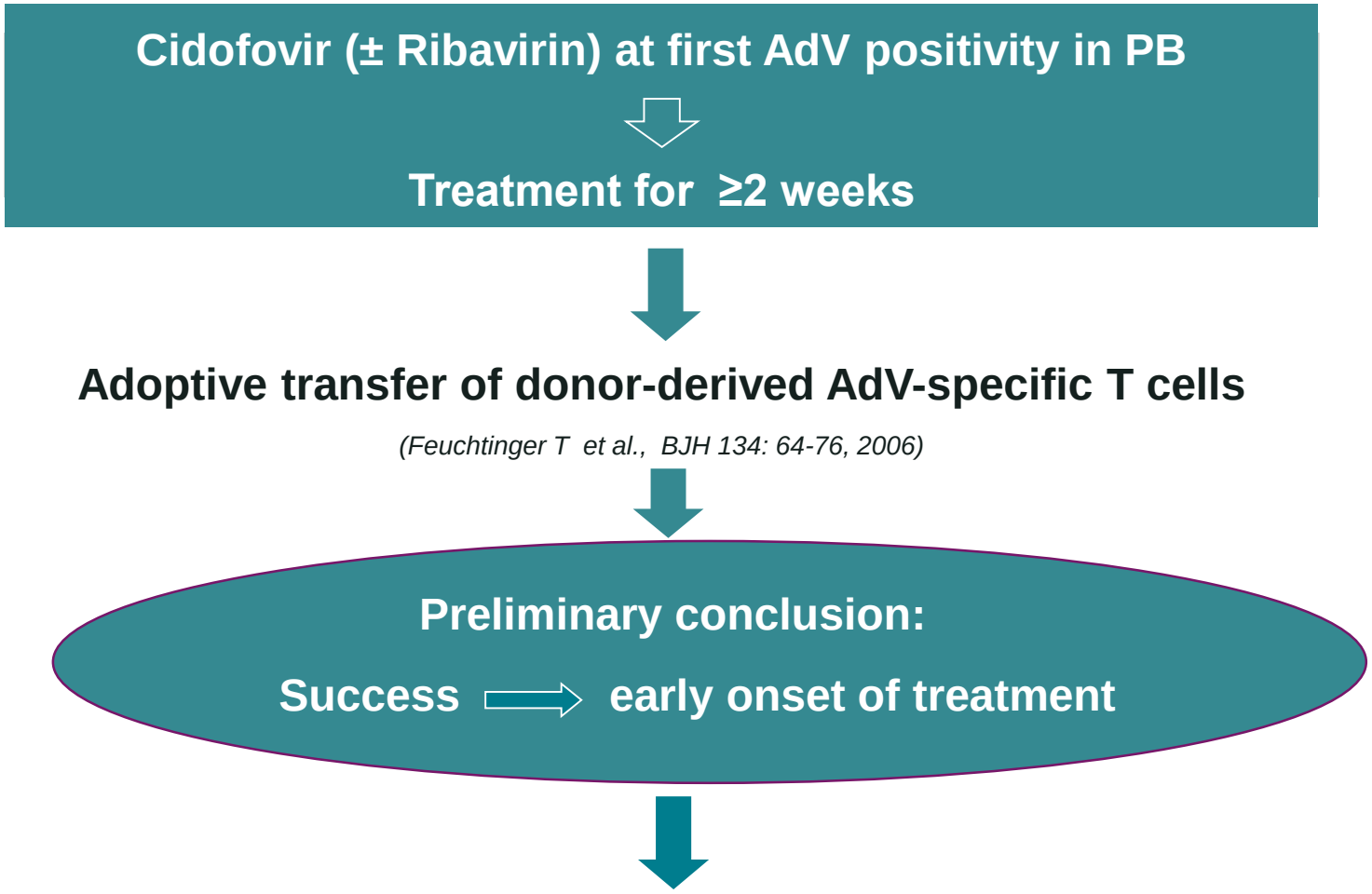
Foscarnet 

no activity

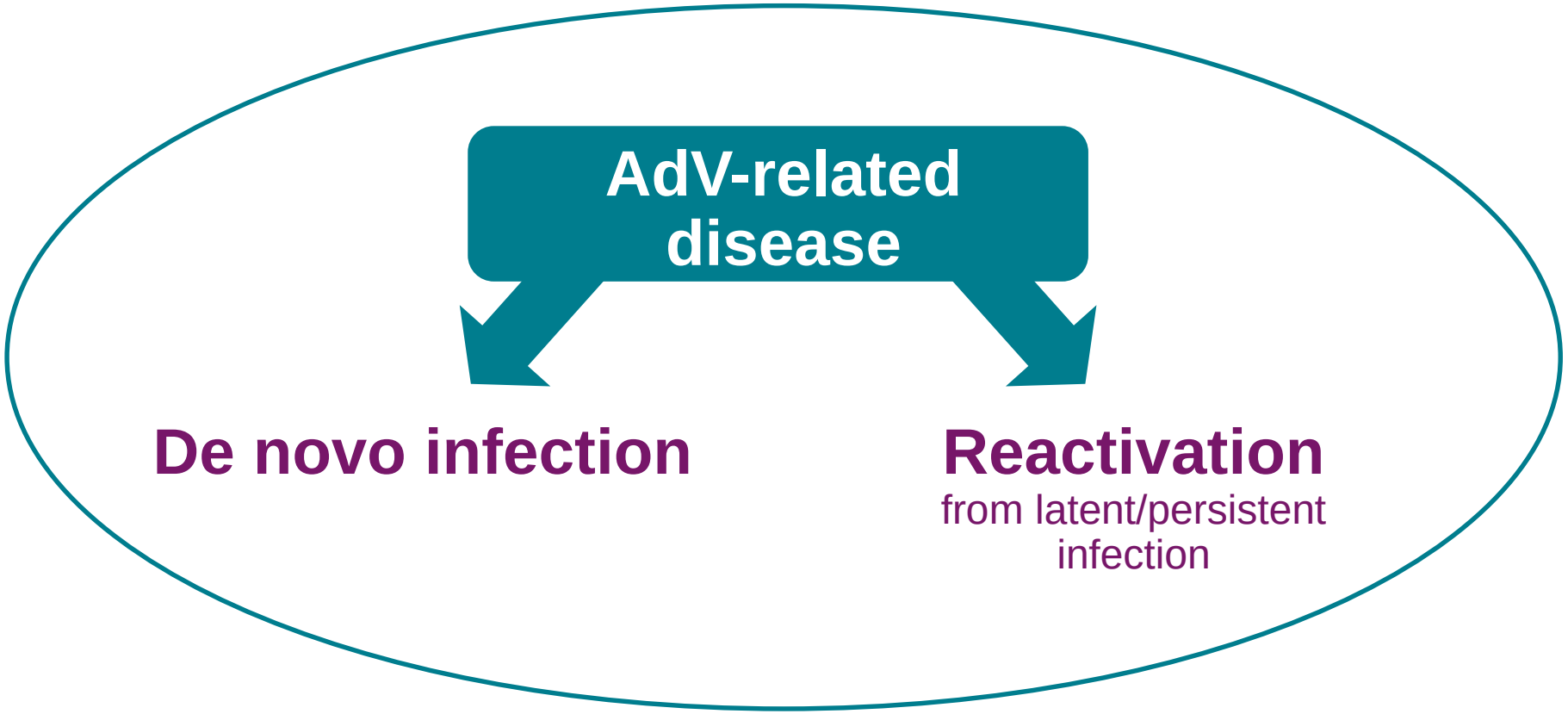
(Naesens L. Antimicrob Agent Ther 2005, 49:1010-16)

* ECIL: European Conference of Infections in Leukemia

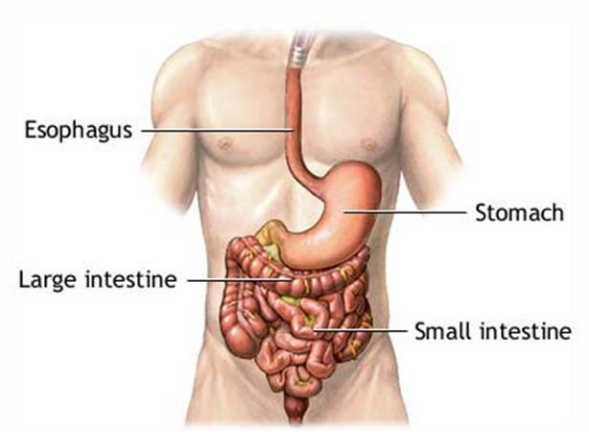
Limited Success of Cidofovir At The Stage of AdV Viremia



What is the Source of AdV Infection in Allogeneic HCT Recipients?



AdV Reactivation from the Gut Drives Disease After HCT



Detection of AdV in stool and viremia

Lion et al. Leukemia 2010, 24(4):706-14

Positivity in stool: 37%

- max. AdV load ≤ $1x10^6$/g
- no/slow replication kinetics

No viremia

(p<0.001)

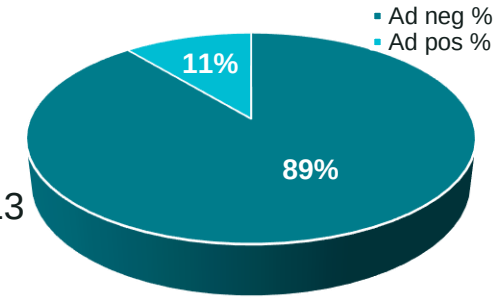
- max. AdV load $5x10^6$-10^{11}/g
- rapid replication kinetics

>70% viremia

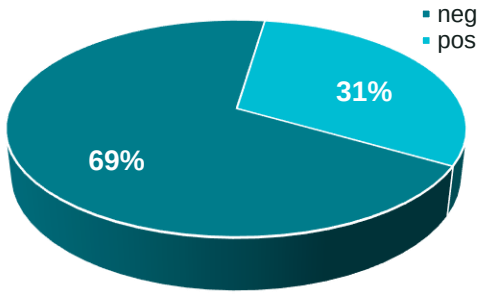
AdV Persists in the Gut of Children

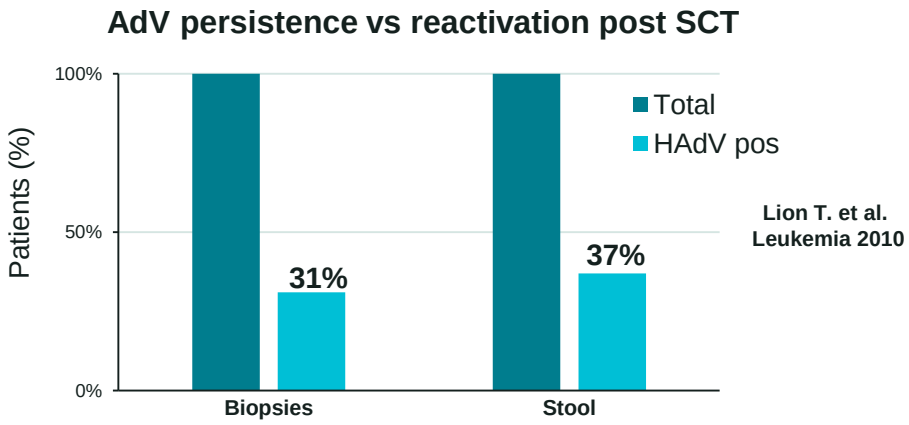
143 immunocompetent children: 576 GI biopsies

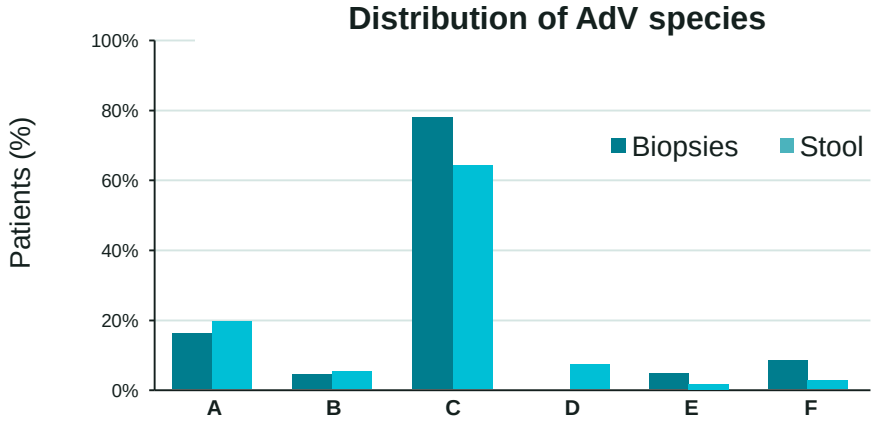
AdV-positive biopsies
pos=63; neg=513



AdV-positive patients
pos=44; neg=99





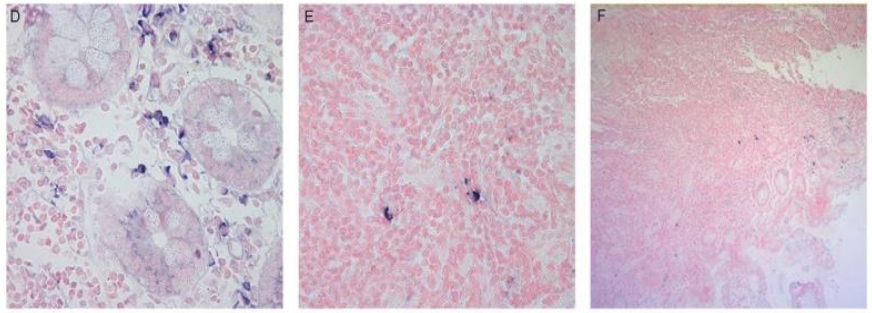


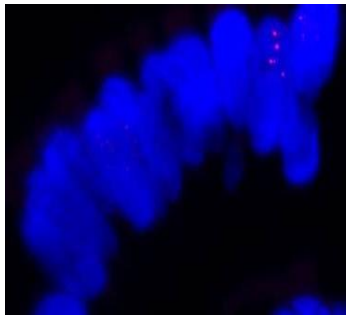
AdV persistence in the GI tract ⟷ risk of reactivation and disseminated disease?

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

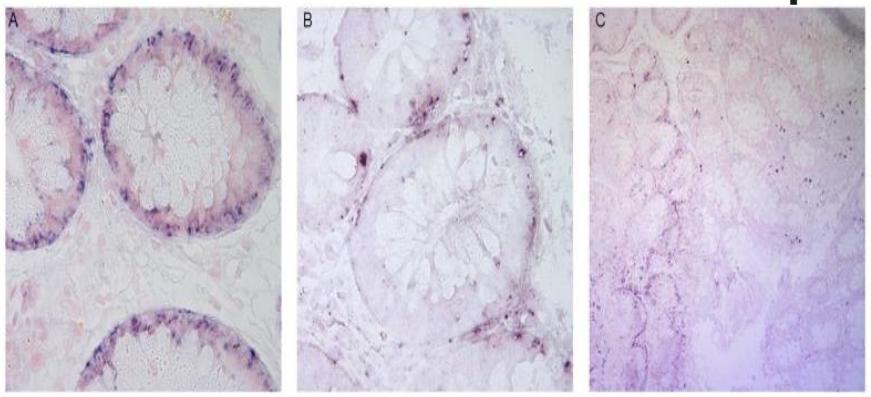
AdV Persists in the Gut of Children and Reactivates from the Gut after Transplant

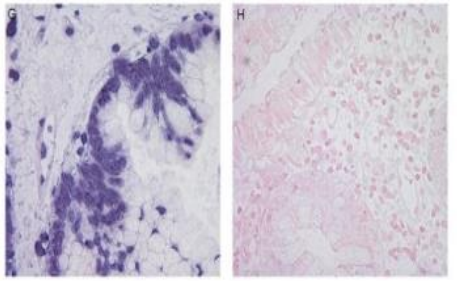
Persistent AdV in gut of immunocompetent children





Reactivated AdV post HCT





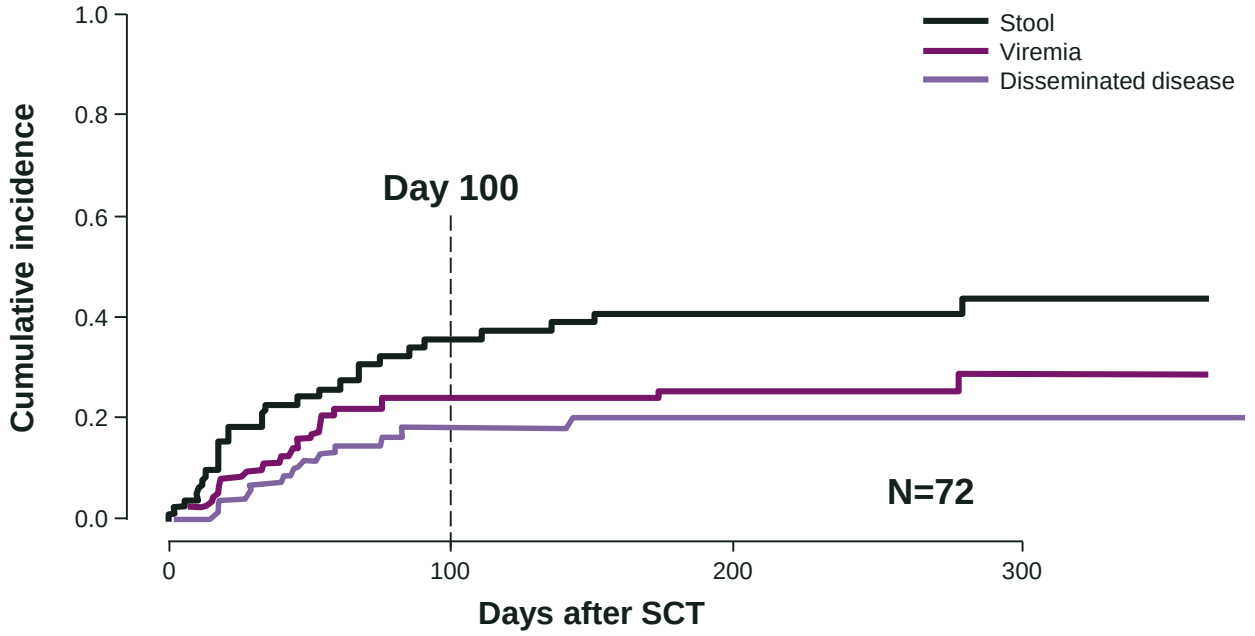
positive control negative control

Presence of virus persistence in the GI tract ➡ intestinal shedding: impact on preemptive AdV treatment strategies in the future?

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

AdV Infection Can Be Detected In Early Post-Transplant Period Stool Followed by Viremia and Disease in First 100 Days[1,2]

Cumulative incidence of adenovirus GI infection, systemic infection, and probable disseminated disease* after HCT in pediatric patients[2]

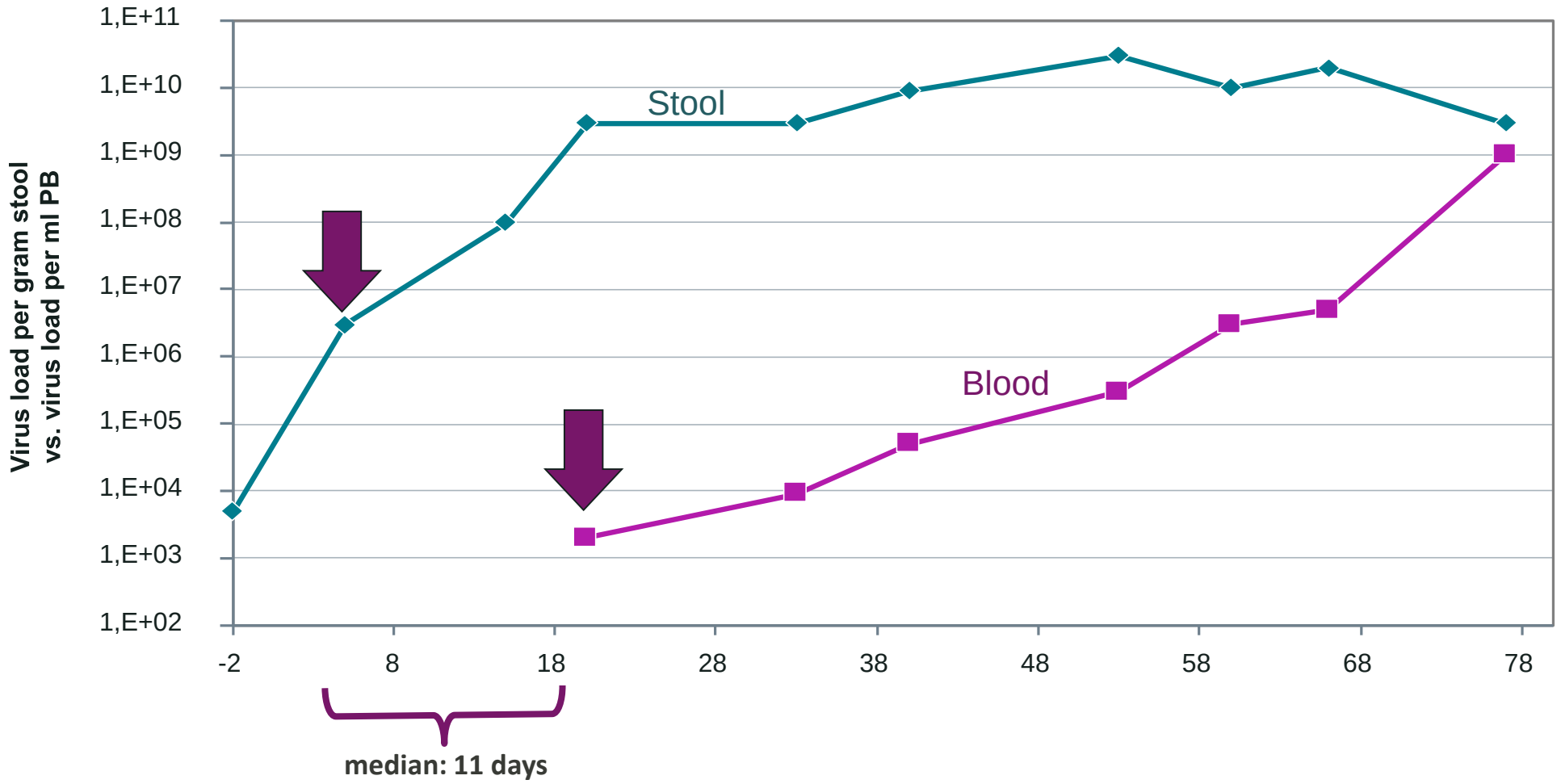


Concomitant reactivation of other DNA viruses e.g. CMV, EBV, HHV6, BKV[2]

*Local digestive infections were defined as positive ADV PCR in stools; systemic infections, as positive ADV PCR in plasma; probable ADV disease, as a systemic infection in association with compatible symptoms, without other identifiable causes.[2]

[1]Bruno B, et al. Biol Blood Marrow Transplant. 2003;9:341-352; [2]Feghoul L, et al. Clin Microbiol Infect. 2015;21:701-709.

Reactivation of AdV in Gut Can Be Easily Monitored in Stool and Predicts AdV Viremia



Lion T. Leukemia 2010, 24(4):706-14; confirmed by Jeulin H et al. Clin Microbiol Infect 2011,17(11):1674-80

Importance of Early Onset of Therapy

Earliest rational employment of antiviral treatment?

- Adenoviremia (currently still ECIL-guideline recommended)
- Intestinal AdV proliferation with stool AdV quantity above the critical threshold
- Intestinal AdV shedding prior to allogeneic HCT

New Therapies Needed for Serious Adenovirus Infections

- IV Cidofovir is nephrotoxic and is used as a bridge until immune-reconstitution
- T-cell therapy is costly, has logistical issues, and has potential for GVHD
  - Study of 26 HCT recipients with disseminated AdV*
    - Only 4 rapid responders, 1/4 were non-responders, all non-responders died
    - No response observed in patients with organ involvement
- New antiviral therapies that can suppress AdV in lymphopenic patients without major toxicity would represent a significant treatment advance

* T. Feuchtinger et al, Blood 2015

ORAL BRINCIDOFOVIR FOR ADENOVIRUS: ADDRESSING THE UNMET NEED

W. Garrett Nichols, MD, MS

Chief Medical Officer

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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 brinci 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
- Short course oral BCV should improve outcomes compared to off-label IV cidofovir
- Brinci has demonstrated hematologic safety in early transplant period and avoids cidofovir-like nephrotoxicity

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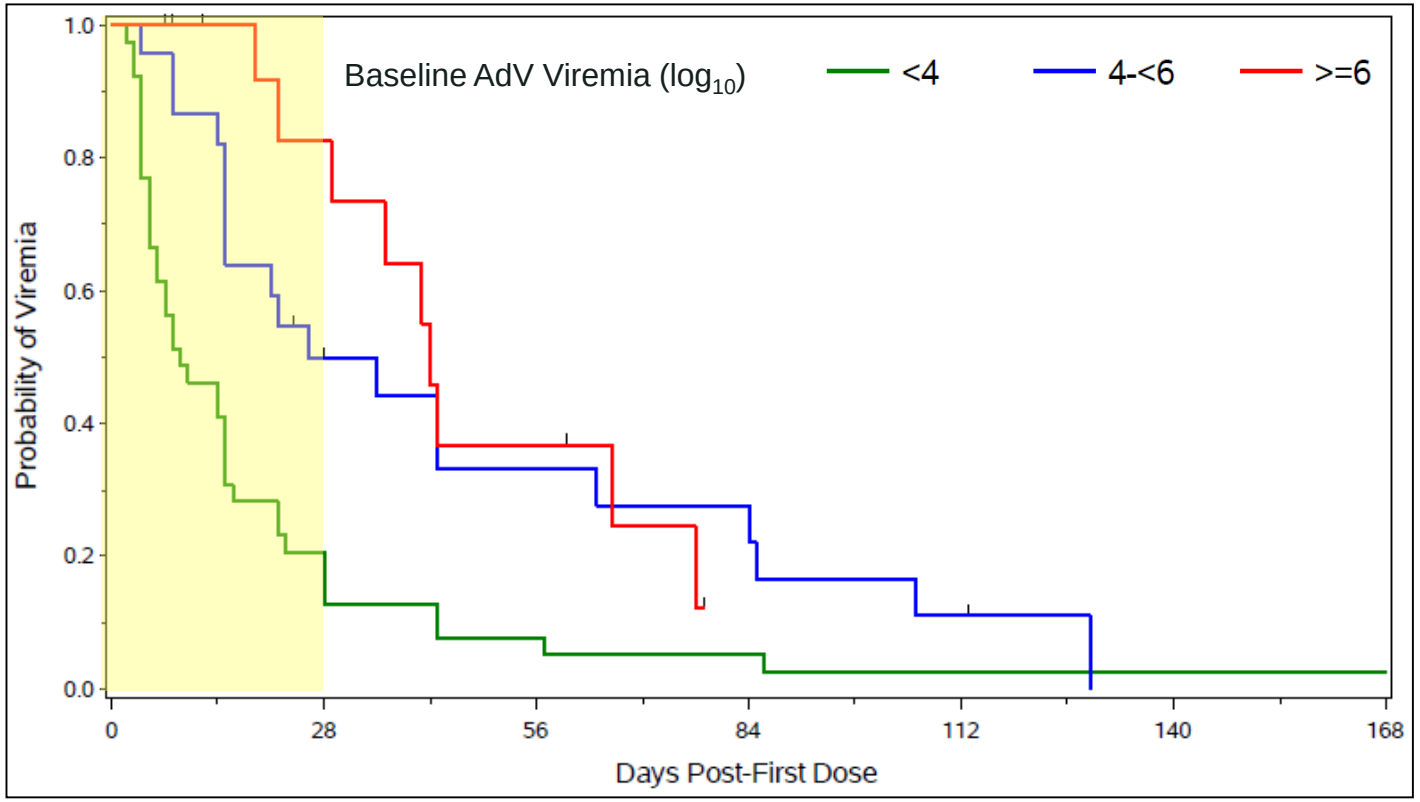
AdVise: Early Intervention Resulted in Undetectable AdV Viral Loads in the First 4 Weeks of Oral BCV

Time to AdV plasma clearance (pediatrics)



- Pediatric pts with lower AdV viral loads at baseline (<10,000 or 4 $\log_{10}$ c/mL) cleared within a median 8 days of oral BCV
- Pediatric pts with AdV <5 $\log_{10}$ c/mL (<100,000): 72% cleared within 4 wks
- AdAPT will enroll at transplant centers that screen for AdV, who are likely to detect and treat AdV viremia while viral loads are ~5 $\log_{10}$ or lower

Short-course Oral BCV should result in clearance of AdV in majority of patients

Prasad V et al. BMT Tandem, Orlando FL, February 2017

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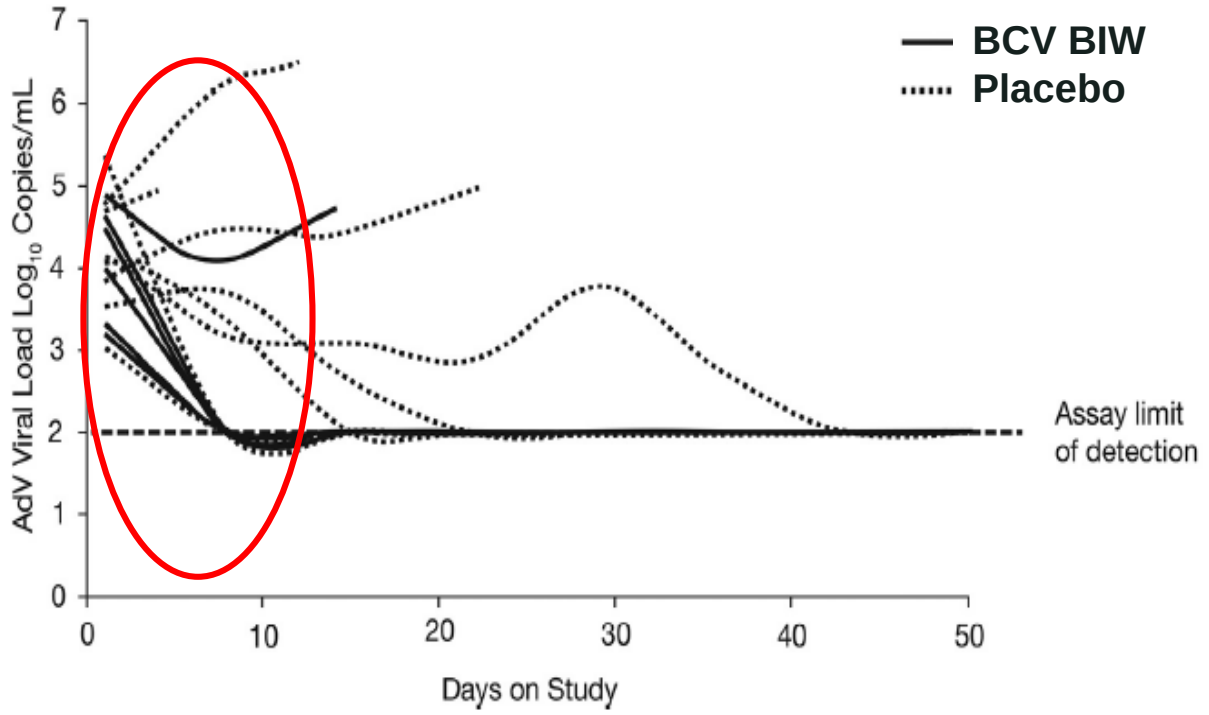
Phase 2 in Asymptomatic AdV: Oral BCV BIW Cleared Plasma in 1 Week if AdV >1000 c/mL

- 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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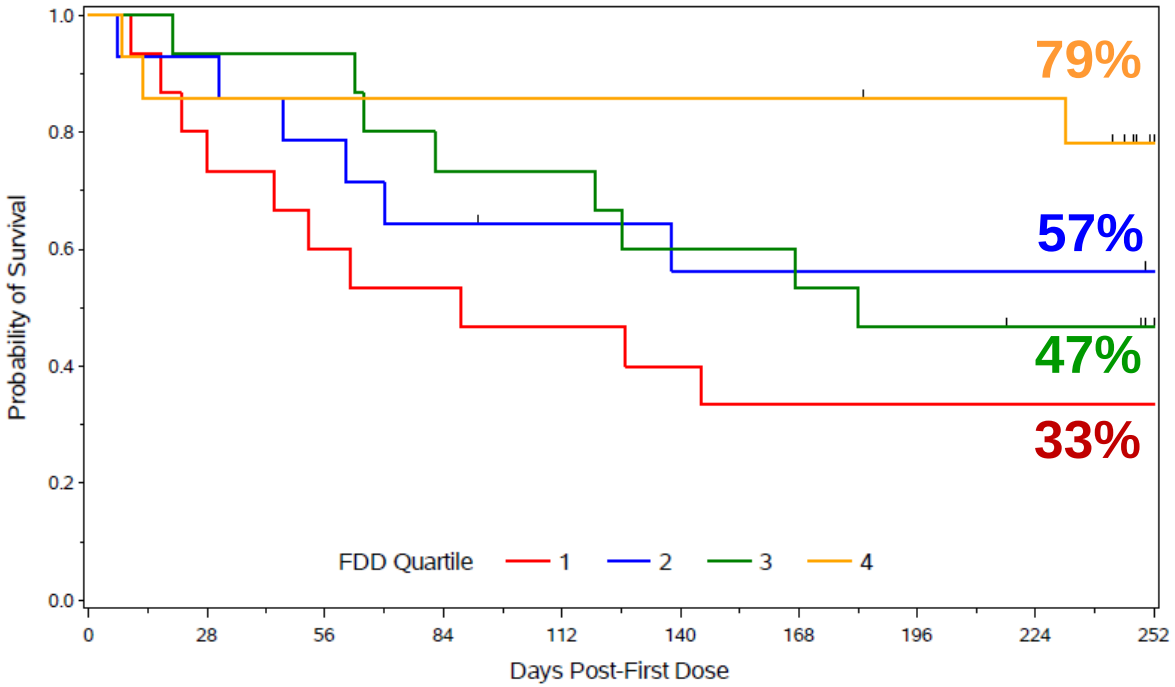
AdVise Highlights the Importance of Early Treatment

- In the first quartile of patients enrolled, patients had extensive prior cidofovir use, high AdV viral load, longest period from diagnosis to first oral BCV dose
- In the final quartile of enrollment, patients received oral BCV more quickly after AdV diagnosis – and had better survival



At Initiation of Oral BCV	First Quartile (n=15)	Fourth Quartile (n=14)
>2 prior doses IV cidofovir	11 (73%)	2 (14%)
Days from AdV diagnosis (median, IQR)	22 (12, 44)	6.5 (4, 9)
AdV BL VL (median, IQR in log_{10} c/mL)	5.4 (3.1, 6.1)	3.6 (2.3, 5.8)

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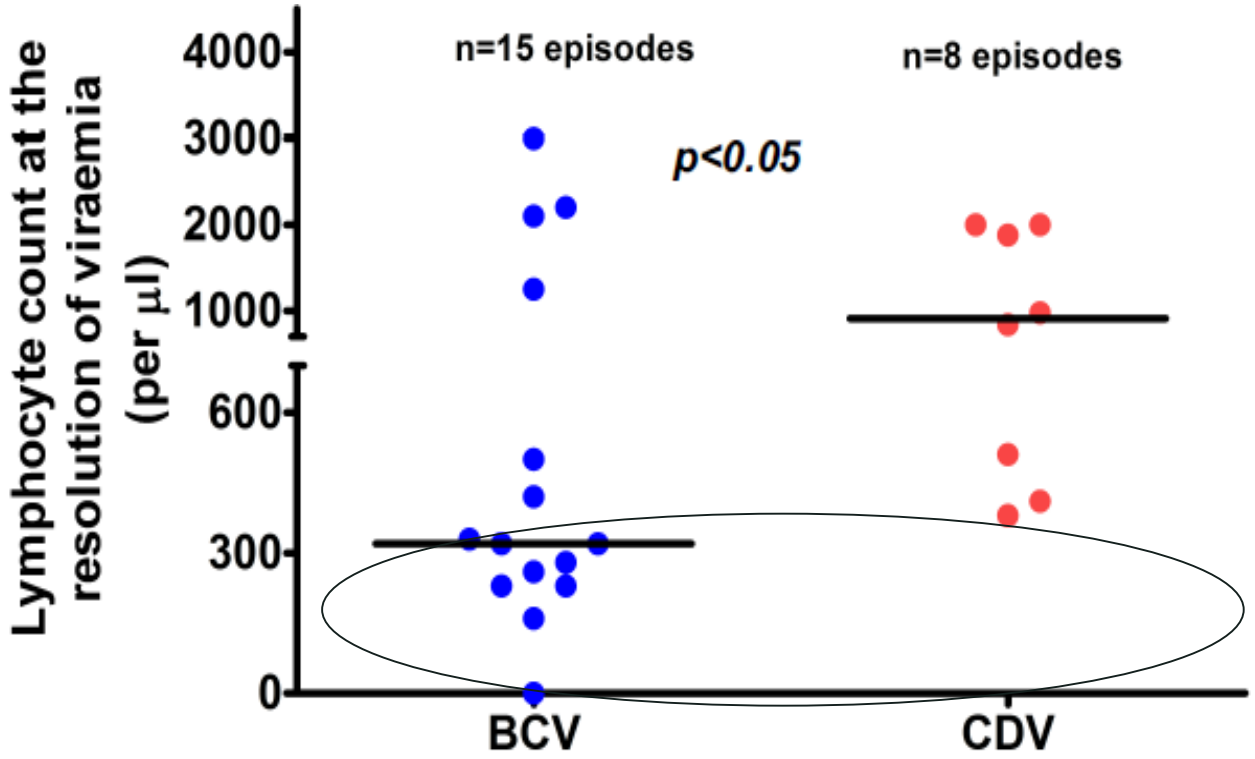
BCV Clears AdV from Plasma with or without Immune Function, While Cidofovir Requires Immune Assistance



- 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]

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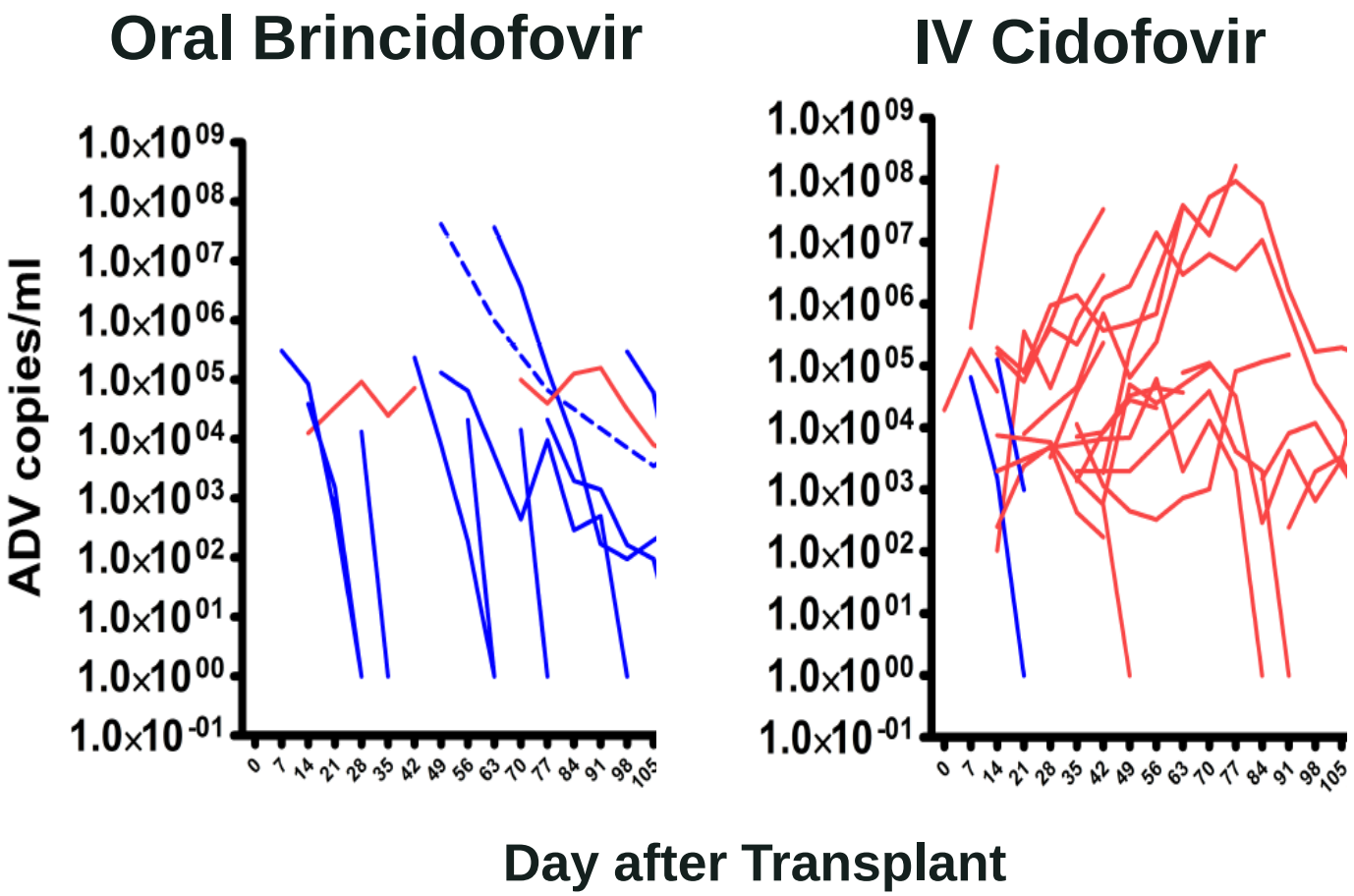
Endpoint of AdV Plasma Clearance at Week 4 Differentiates Oral BCV from Off-Label IV Cidofovir



- 80% of pediatric HCT patients cleared with BCV (median 4 wks)
  - Only 35% cleared with IV CDV (median 9 wks)
- Differences were greatest in first 100 days post-HCT (before immune reconstitution)
- Differentiated safety:
  - With short course therapy only 1/18 discontinued BCV for GI AEs
  - Cidovfovir: renal toxicity observed in 9/23 patients

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

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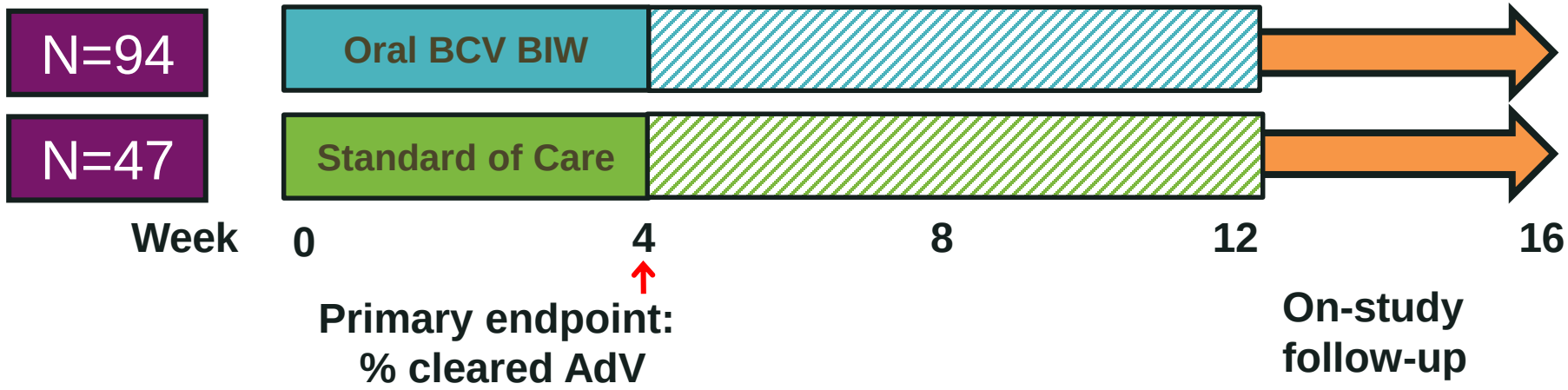
AdAPT: Adenovirus after Allogeneic Pediatric Transplantation

- **Small, open label, comparative study** of Oral BCV vs. standard of care (SoC)
  - Inclusion: pediatric T-cell depleted allogeneic HCT recipients with confirmed >1000 c/mL AdV DNA in plasma, <100d from HCT
- **Short course therapy**: Treat until AdV cleared from plasma (min 4 weeks, max 12 weeks)
  - Preemptive approach well established for other viral infections (e.g., CMV)
- **Primary endpoint: % undetectable plasma AdV at Week 4**
  - N~140 (2:1, 90% power) for 70% oral BCV vs. 40% SoC response rate
  - Superiority of oral BCV in clearance of AdV from plasma could enable conditional or full EU Approval



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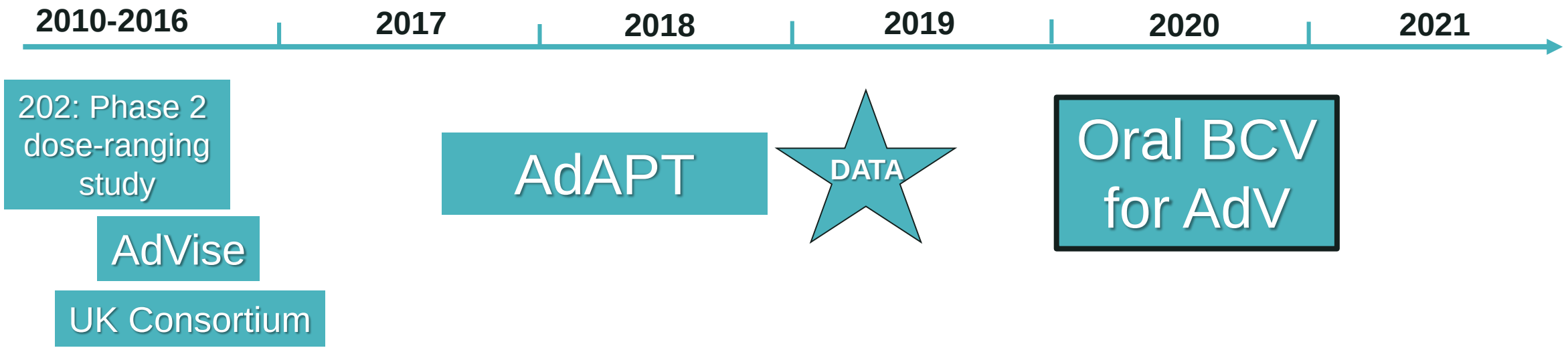
Oral Brincidofovir for Treatment of AdV: Development and Approval Timelines



- AdAPT has been designed together with European regulators to provide a small randomized study of oral BCV for short-course treatment of AdV
- AdAPT should provide data sufficient for a conditional or full approval

All timelines are estimated

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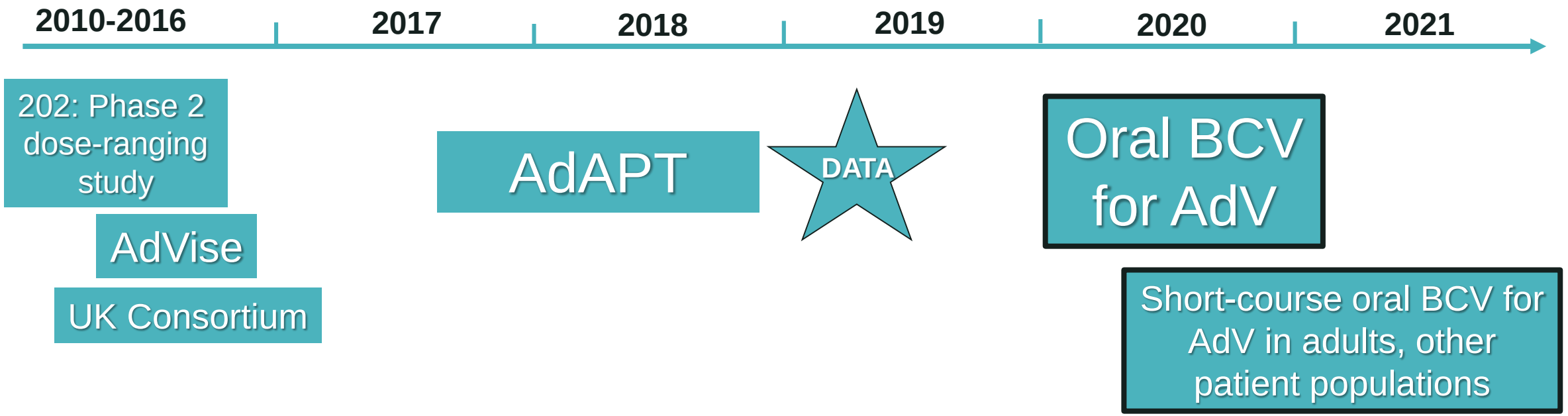
Oral Brincidofovir for Treatment of AdV: Development and Approval Timelines



- AdAPT has been designed together with European regulators to provide a small randomized study of oral BCV for short-course treatment of AdV
- AdAPT should provide data sufficient for a conditional or full approval
- Additional patient populations with serious AdV infections will be studied

All timelines are estimated

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Proposed Indication for Short-course Oral BCV in EU

- “Brincidofovir is indicated in children from 2 months of age for:
  - the treatment of adenovirus disease in immunocompromised patients, and
  - the prevention of adenovirus disease in stem cell transplant recipients with adenovirus viremia”

Next steps:

- EU: Final Protocol and background package submitted to CHMP to confirm study is sufficient for conditional approval in EU – anticipate feedback by end of July
- US: AdAPT protocol will be submitted to FDA for conduct in US
  - Following data availability, and potentially with a positive opinion from EMA, consider petition of FDA for consideration of data for accelerated approval

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THE IMPACT OF MULTIPLE DNA VIRAL INFECTIONS AFTER ALLOGENEIC HCT

Joshua A. Hill, MD

Associate, Vaccine and Infectious Disease Division

Fred Hutchinson Cancer Research Center

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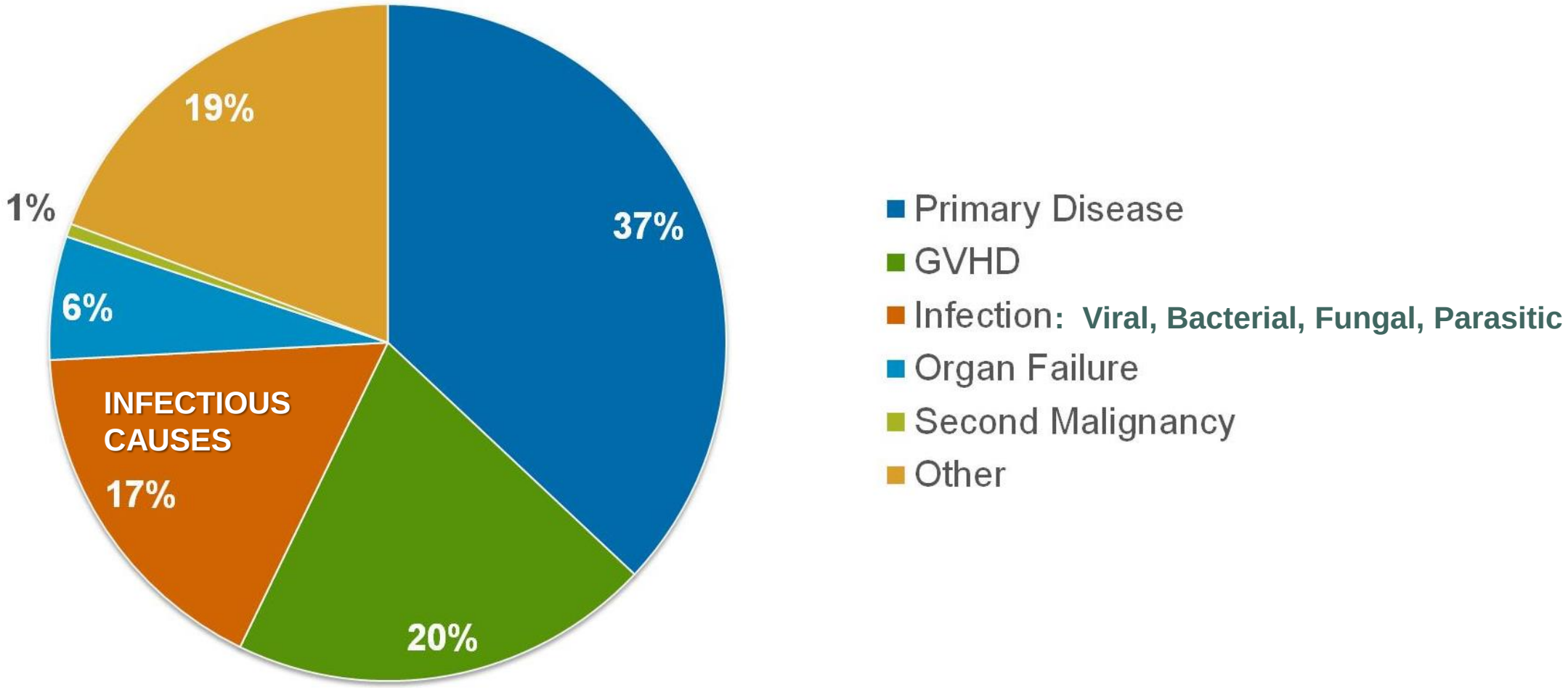
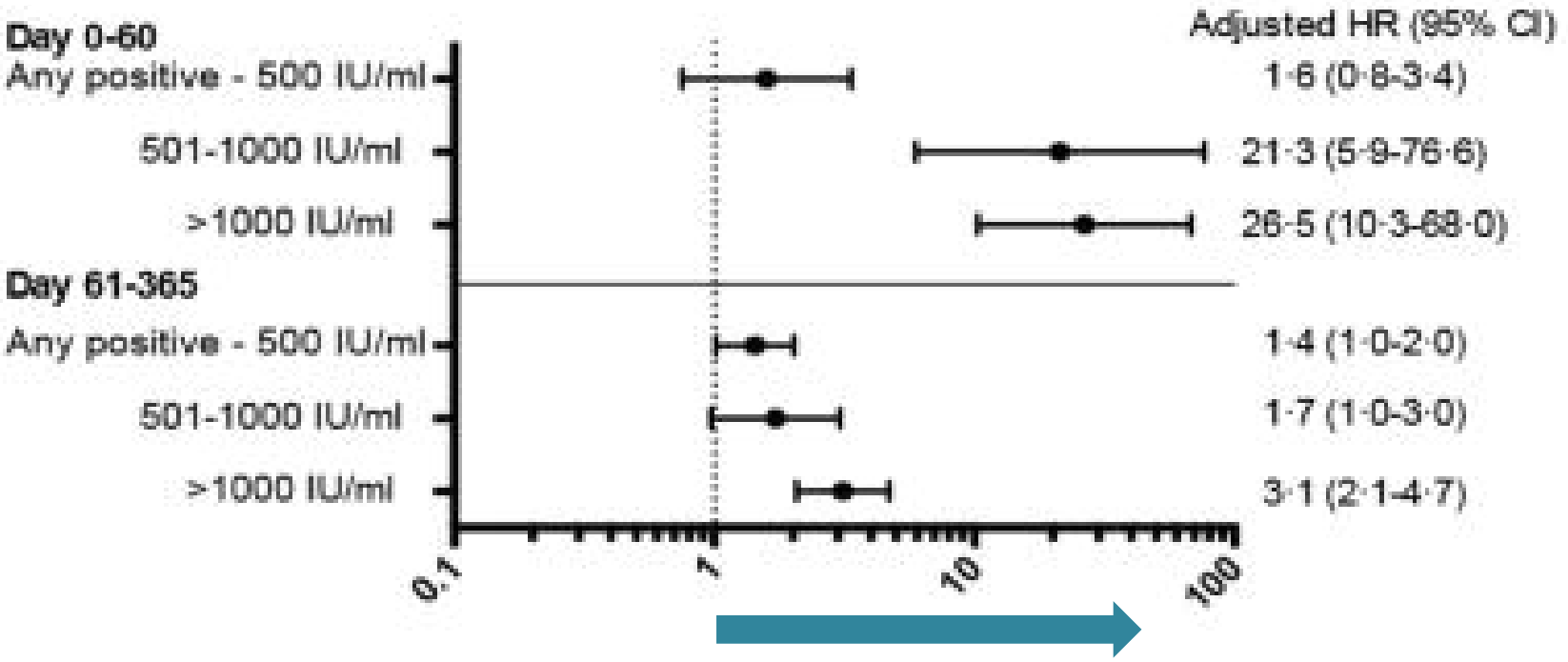
Infections Remain a Frequent Cause of Death After Bone Marrow Transplantation



Source: CIBMTR

Reactivation of Even A Single DNA Virus Increases Mortality Risk Despite Current Screening and Prevention Strategies



- Following Allo-HCT even a single positive CMV PCR increases mortality risk

Green et al, Lancet Heme 2016

Objectives of Study

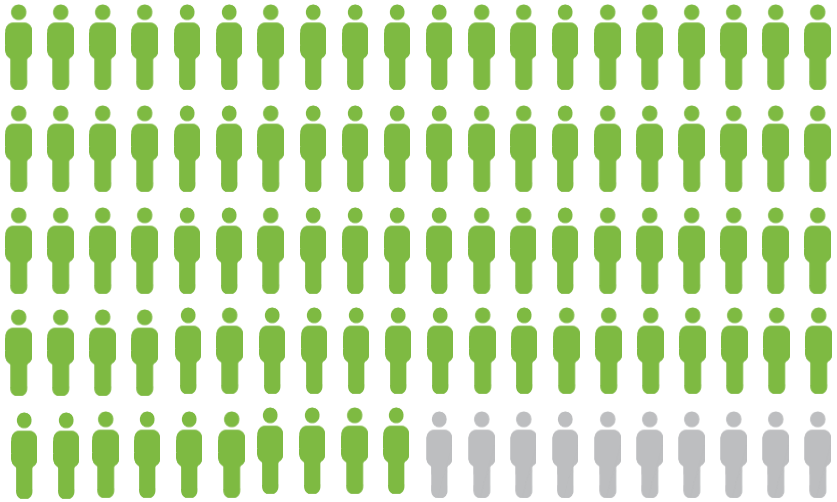
- To determine the epidemiology of plasma detection of 5 DNA viruses within the first 100 days after allogeneic HCT in a contemporary cohort
  - CMV, HHV-6, EBV, BKV, AdV
- To assess the cumulative impact of multiple DNA viruses on HCT outcomes
- To describe the kinetics of viral detection post-HCT

No prior study has looked comprehensively at DNA virus reactivation after HCT

Study Design

- Retrospective analysis of stored sera from 404 HCT recipients at FHCRC
- Consecutive allo-HCT patients between 2007-2014 (1,926 patients eligible)
  - 125 cord blood
  - 125 HLA-mismatched (including 47 haploidentical donors)
  - 154 HLA-matched
- Banked plasma samples were tested for BKV, HHV-6, AdV, and EBV
  - CMV results were obtained from routine clinical testing
- Inclusion criteria
    - First allogeneic HCT recipient (all ages)
    - First available plasma sample obtained before day 21
    - ≥60% of weekly plasma samples available to day 100 post-HCT (or death if at <100 days)

90% of Allo-HCT Had At least one DNA Virus Detected

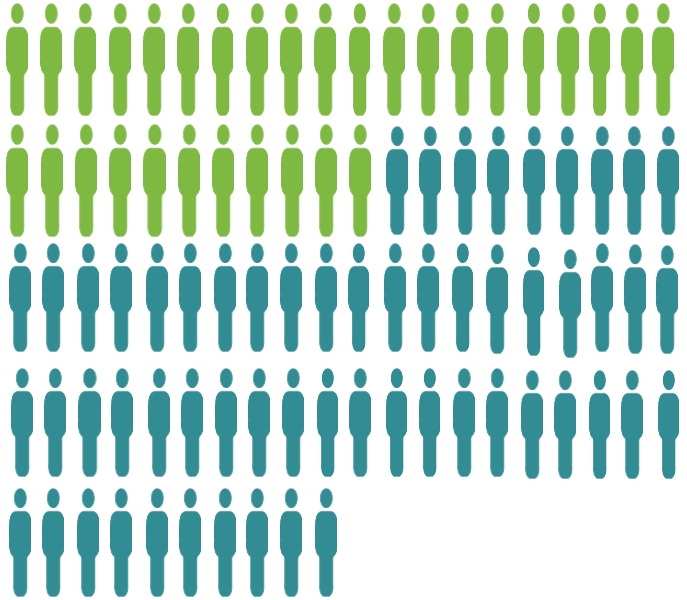


At least one DNA Virus in 363/404=

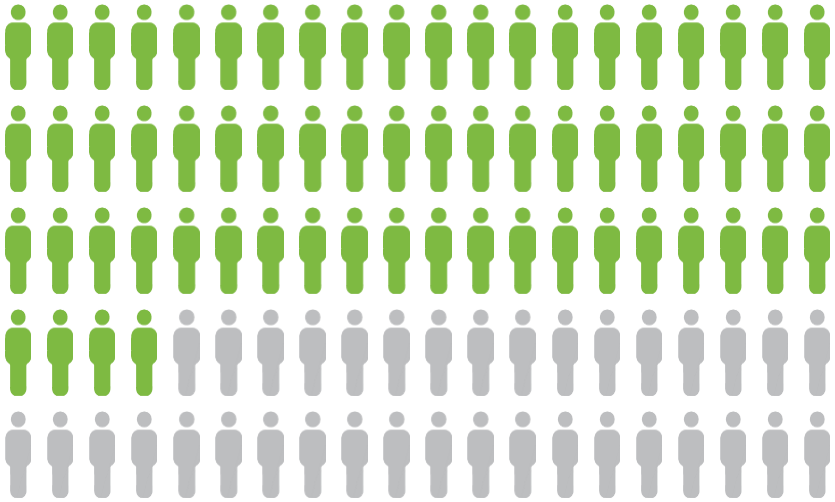
90%

2/3 have two or more DNA viruses

66%



2/3 of Patients Reactivated CMV, Usually With Another DNA Virus



CMV in 260/404=

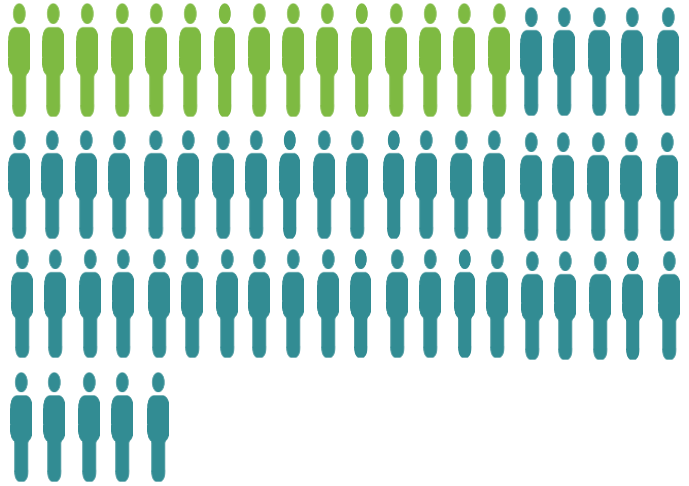
64%

CMV only 63/260

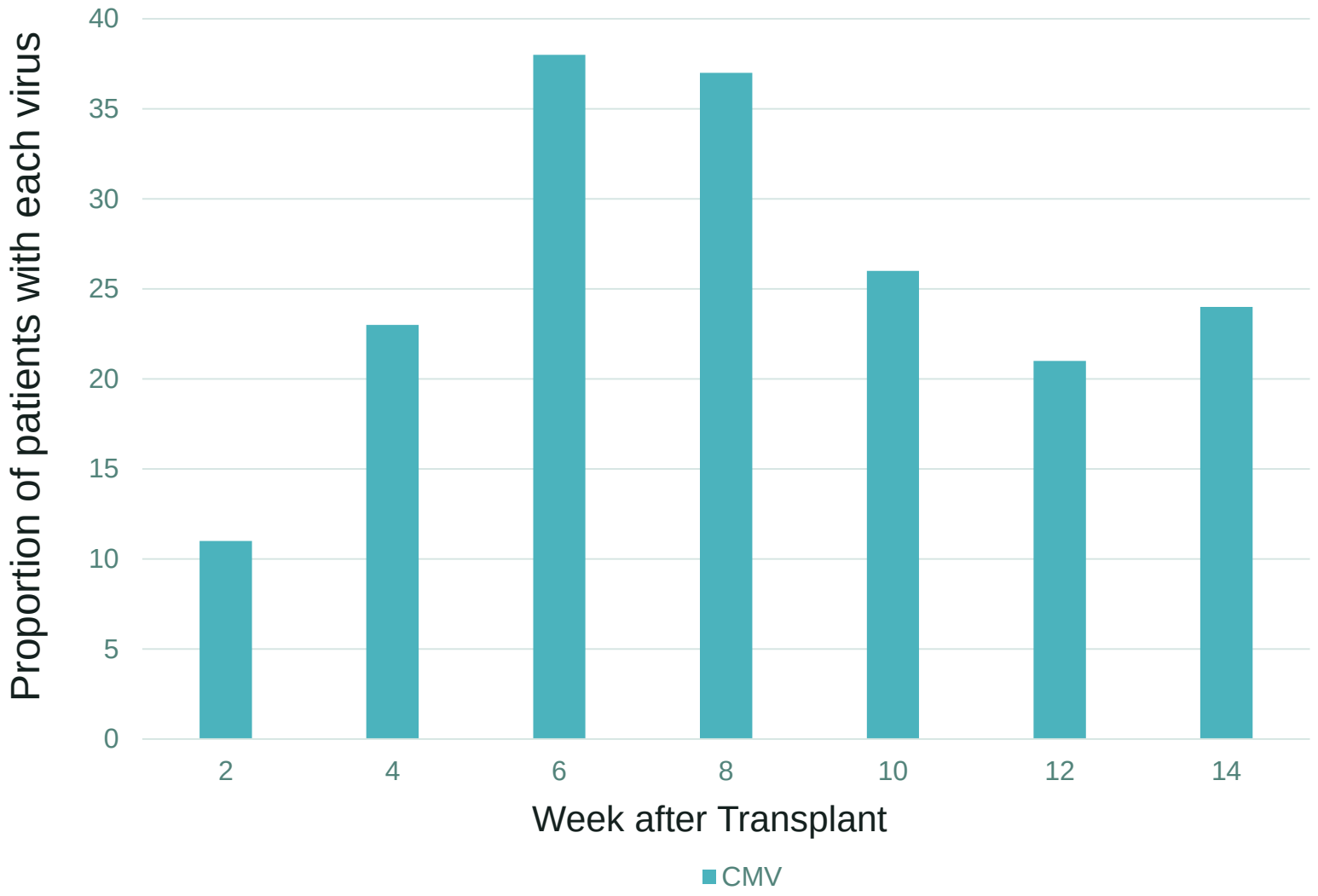
24%

CMV + one or more other viruses

76%



Viruses Reactivate Early and Persist

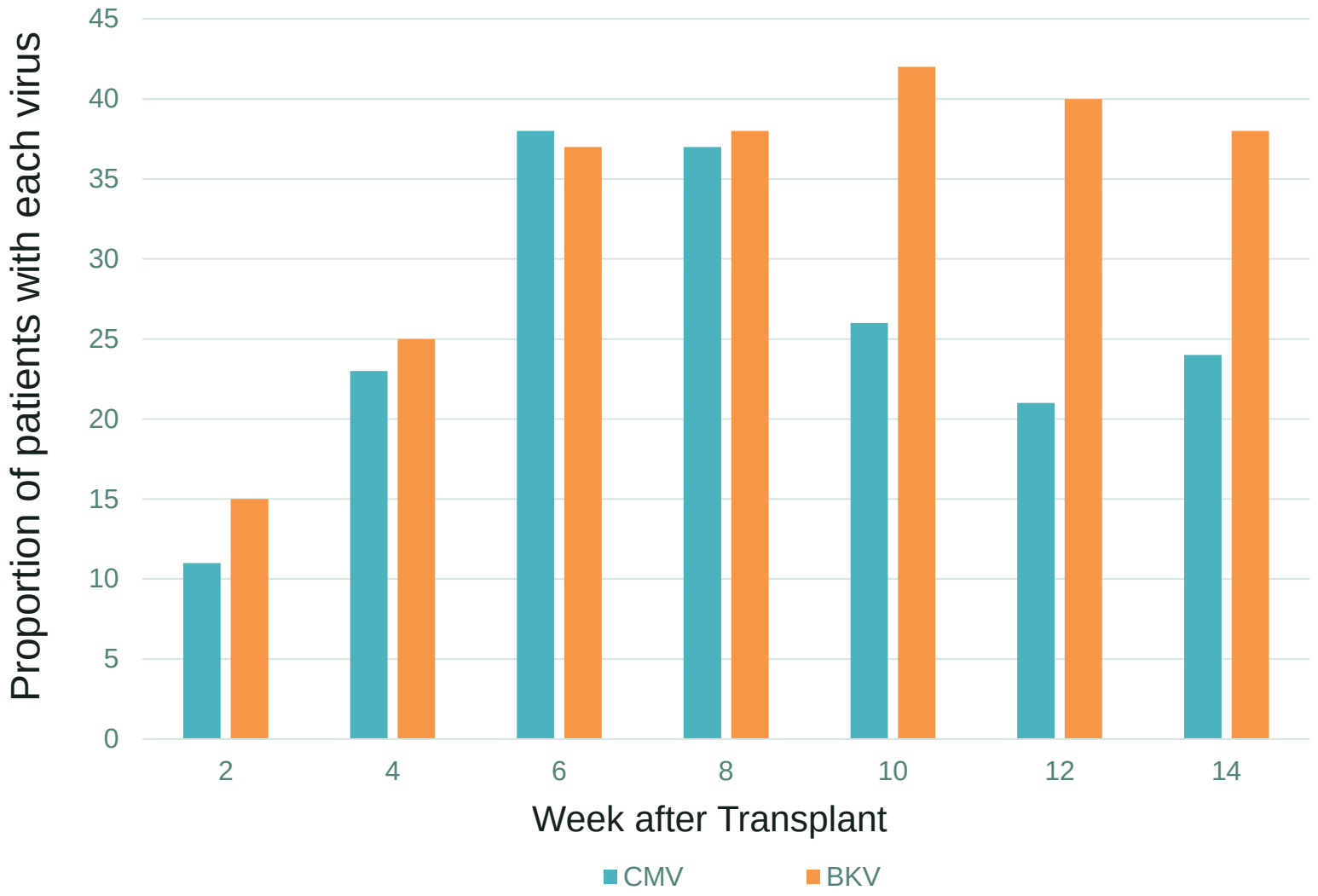


Cumulative Incidence First 100 Days:

CMV 64%

Hill et al, BMT Tandem meeting 2016

Viruses Reactivate Early and Persist



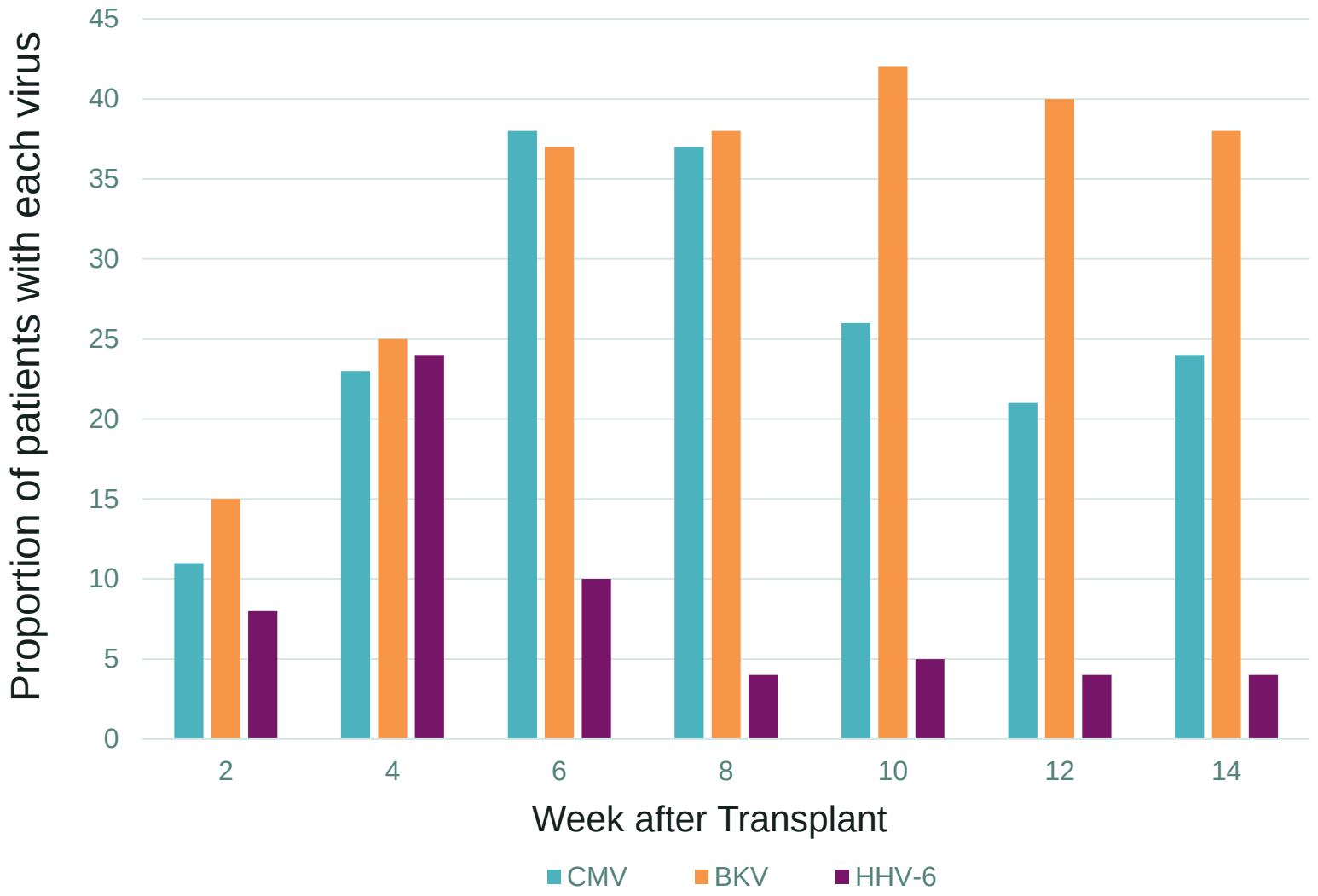
Cumulative Incidence First 100 Days:

CMV 64%

BKV 54%

Hill et al, BMT Tandem meeting 2016

Viruses Reactivate Early and Persist

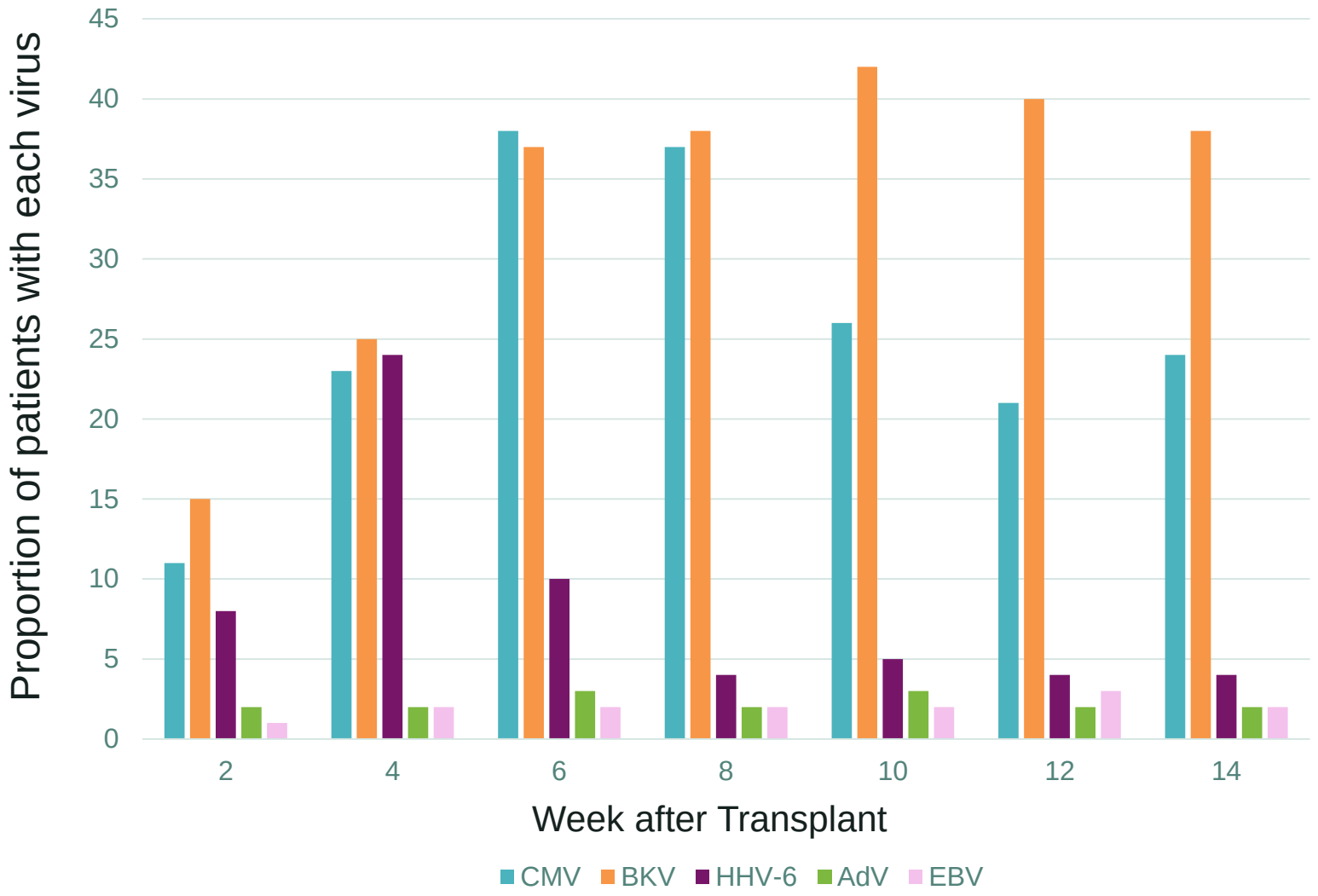


Cumulative Incidence First 100 Days:

CMV	64%
BKV	54%
HHV-6	47%

Hill et al, BMT Tandem meeting 2016

Viruses Reactivate Early and Persist

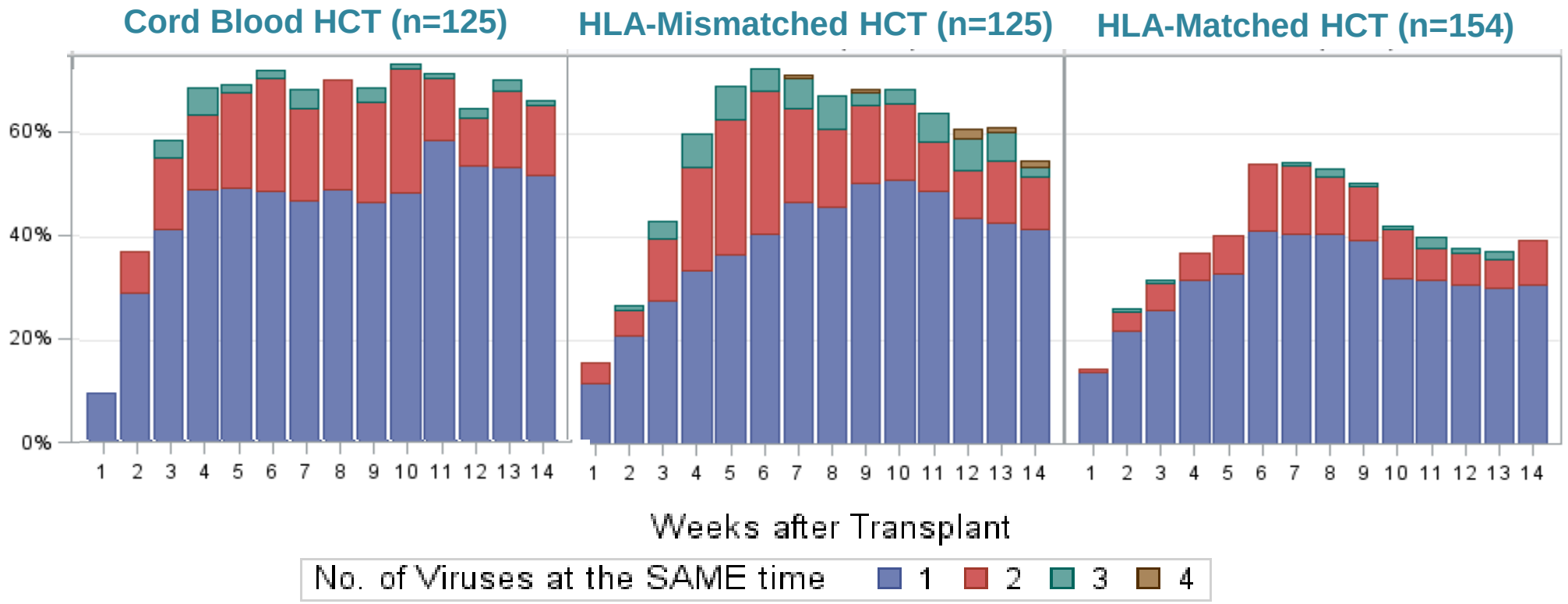


Cumulative Incidence First 100 Days:

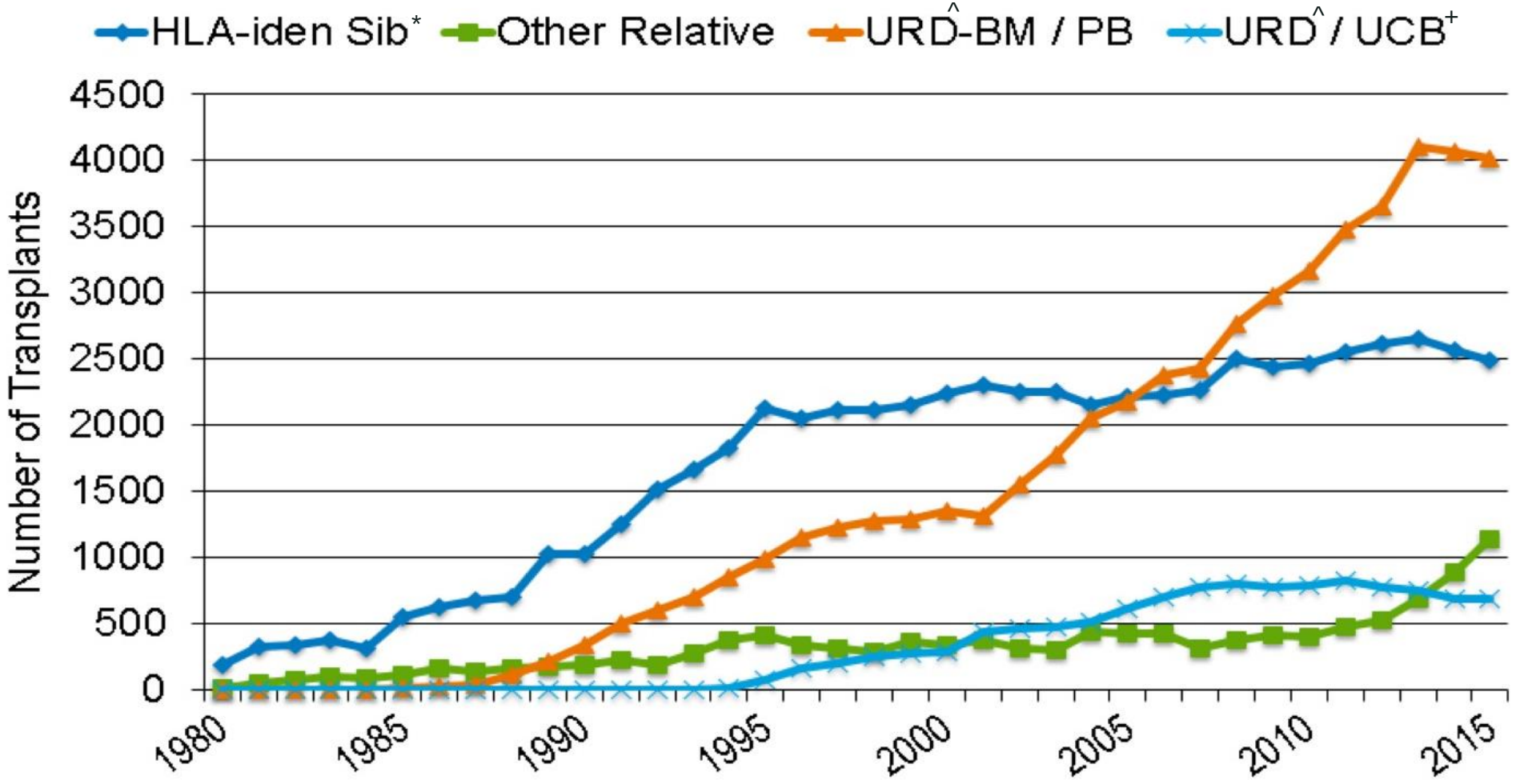
CMV	64%
BKV	54%
HHV-6	47%
AdV	10%
EBV	9%

Hill et al, BMT Tandem meeting 2016

Multi Viral Reactivation More Common in High Risk HCT but Also Occurs in ~50% of Matched Allogeneic Transplants



Increasing Rate of High Risk Allo-HCT is Driving Growth

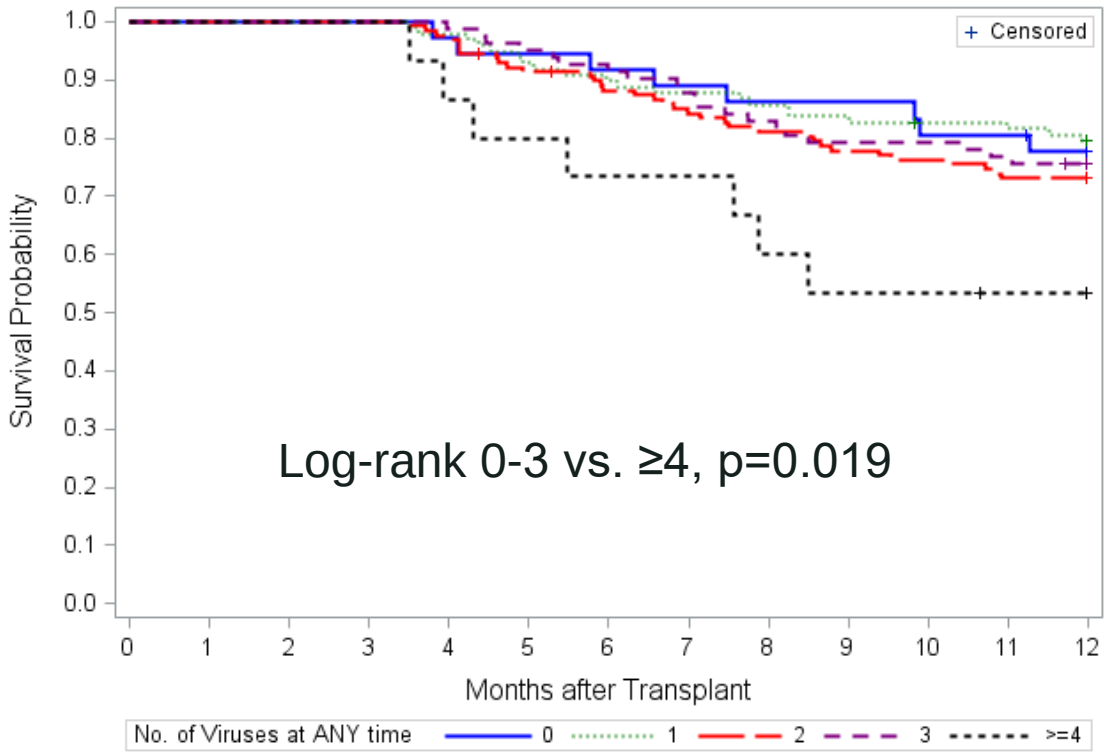


* Identical Sibling ^ Unrelated Donor + Unrelated Cord Blood

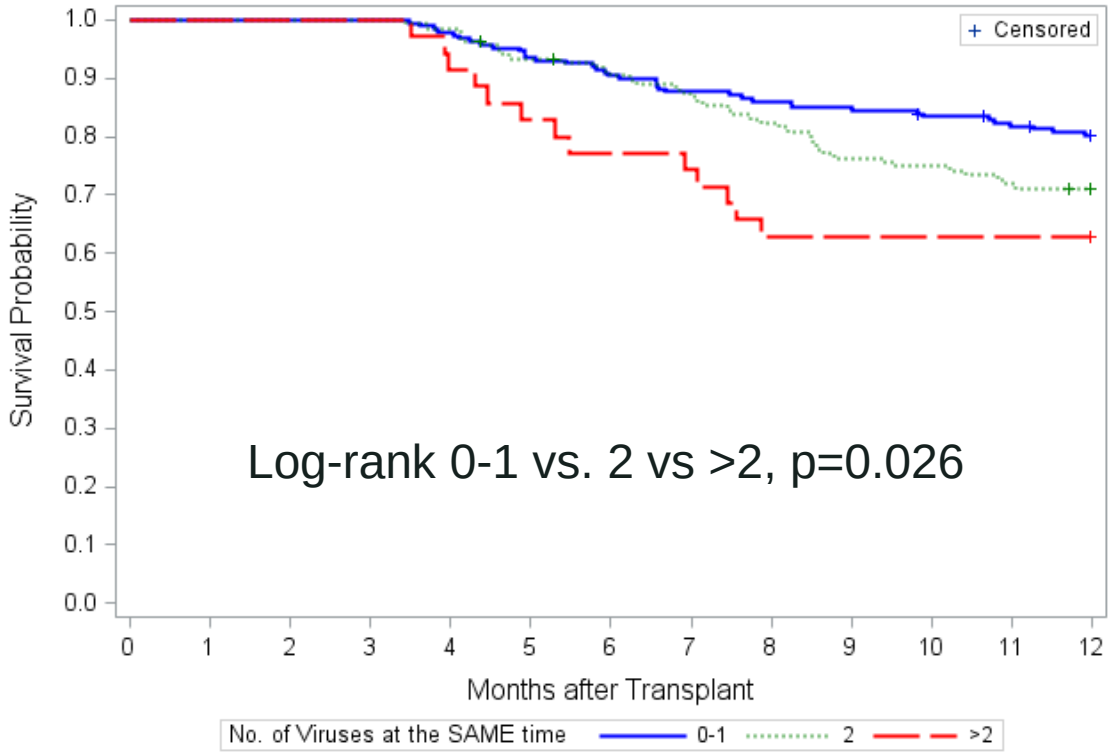
Source: CIBMTR

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

DNA Viral Burden Increases Hazard of Overall Mortality In the First Year after HCT

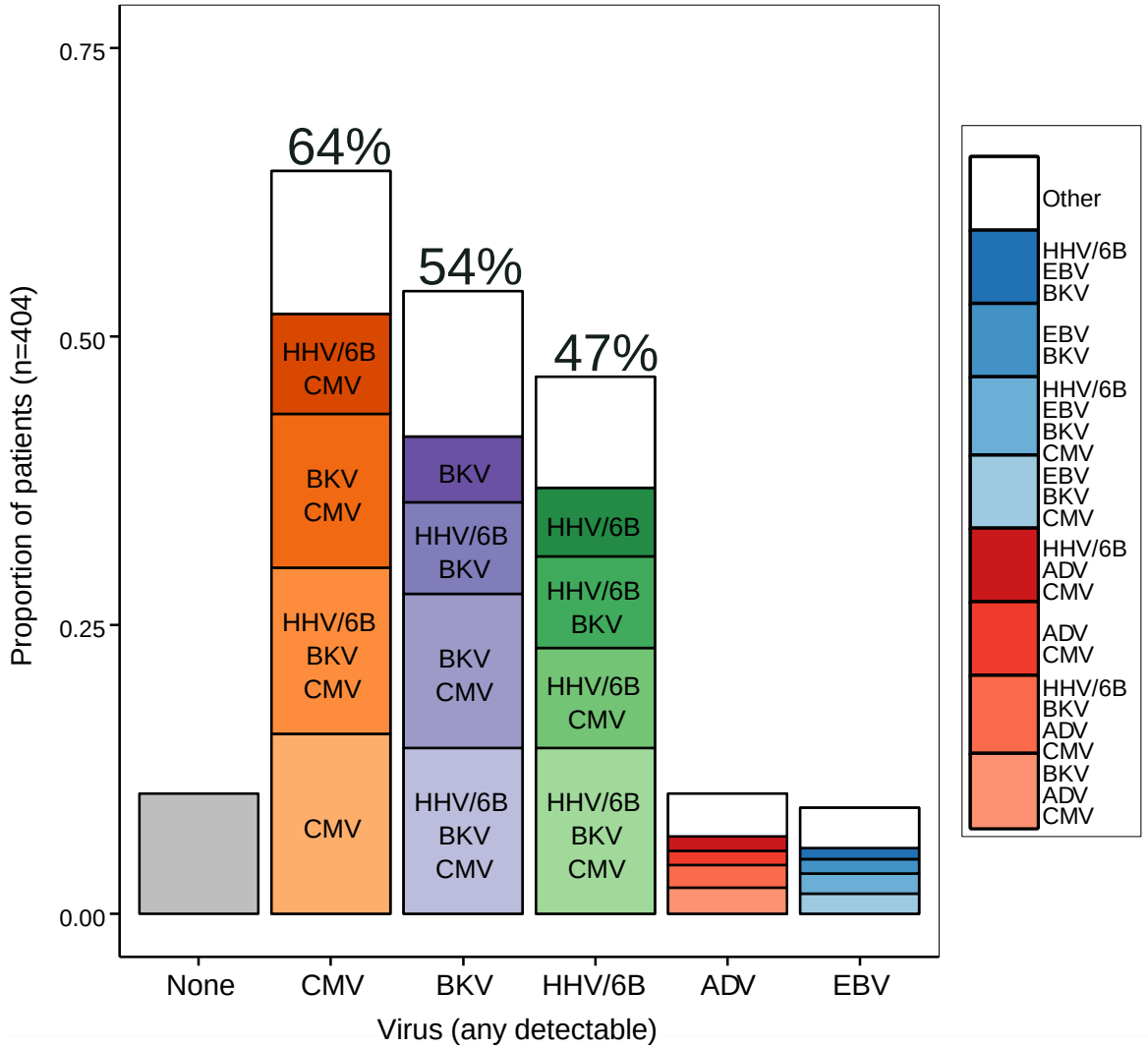
Virus	Risk Period	Adjusted HR (95% CI)
CMV	Day 0-100	1.45 (1.18-1.79)
	Day 101-365	1.08 (1.00-1.17)
BKV	Day 0-100	1.25 (1.06-1.46)
	Day 101-365	0.95 (0.89-1.02)
HHV-6	Day 0-100	1.08 (0.78-1.50)
	Day 101-365	1.28 (1.13-1.46)
AdV	Day 0-100	1.95 (1.27-3.00)
	Day 101-365	1.14 (0.88-1.47)
EBV	Day 0-100	7.80 (4.86-12.5)
	Day 101-365	0.98 (0.61-1.56)

Adjusted Hazard Ratio (HR) for age, HCT comorbidity index score, underlying disease risk, conditioning regimen, acute graft-versus-host disease grade 3-4, and steroid dose during the first 100 days post-HCT

Hill et al, IDWeek 2016

Conclusions: DNA Viruses Reactivate Frequently and In Combination After Allo-HCT

- DNA viral activations were frequent after HCT, despite current strategies
- CMV is frequent but rarely occurs on its own
- Cumulative burden of DNA viruses was associated with increased mortality
  - Increased mortality was independent of poor immune reconstitution and acute GVHD
- Data demonstrate the need for novel strategies to prevent multiple DNA viral infections and their negative impact on outcomes



IV BRINCIDOFOVIR: EMERGING DATA AND DEVELOPMENT PLANS FOR MULTI-VIRAL PREVENTION IN HCT RECIPIENTS

W. Garrett Nichols, MD, MS

Chief Medical Officer

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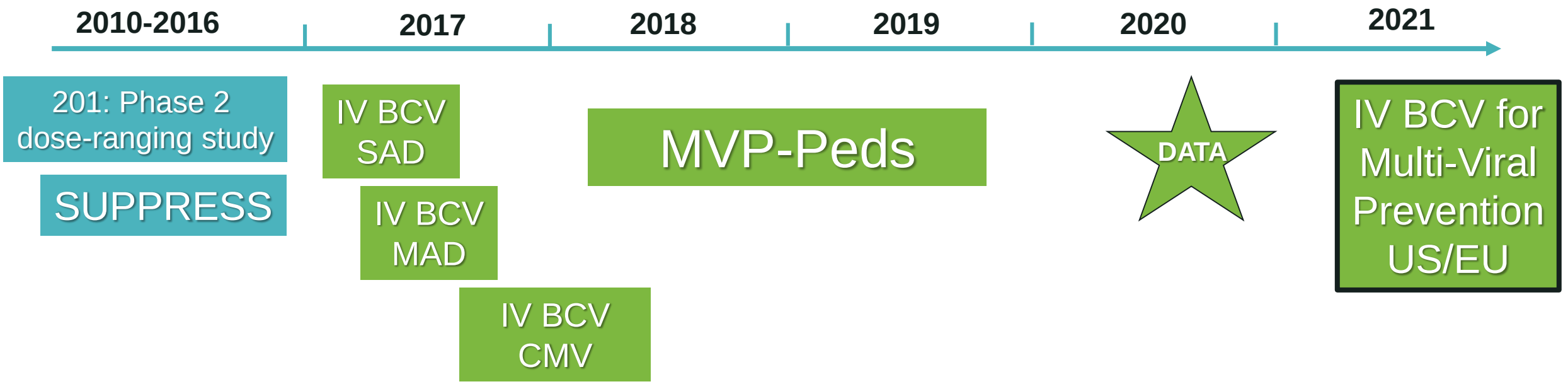
IV Brincidofovir for Multi-Viral Prevention in HCT Recipients: Development and Approval Timelines



- MVP-Peds provides the opportunity to demonstrate the importance of preventing multiple DNA viral infections in a placebo-controlled superiority pivotal study

All timelines are estimated

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IV BCV Single Ascending Dose Design Overview

- Objectives
  - Determine IV BCV dose that delivers similar exposure as 100 mg oral BCV
  - Evaluate CDV-PP (active antiviral) concentration in peripheral blood mononuclear cells, and association with plasma BCV Cmax and AUC
  - Determine safety/tolerability of IV BCV, and association of AEs with PK parameters
  - Explore supratherapeutic drug exposures to rule out QT effects and other potential safety signals

Cohort	N	Planned Doses
"Therapeutic doses"		
1	6 active / 2 placebo	• IV BCV 10 mg or IV placebo • Single dose • 2 hour infusion
2	6 active / 2 placebo	• IV BCV 25 mg or IV placebo • Single dose • 2 hour infusion
"Supratherapeutic" doses		
3	9 active/ 3 placebo	• IV BCV 50 mg or IV placebo • Single dose • 2 hour infusion
4	9 active / 3 placebo	• IV BCV 50 mg or IV placebo • Single dose • **4 hour infusion**

Participants were healthy males, mean age ~ 25 years

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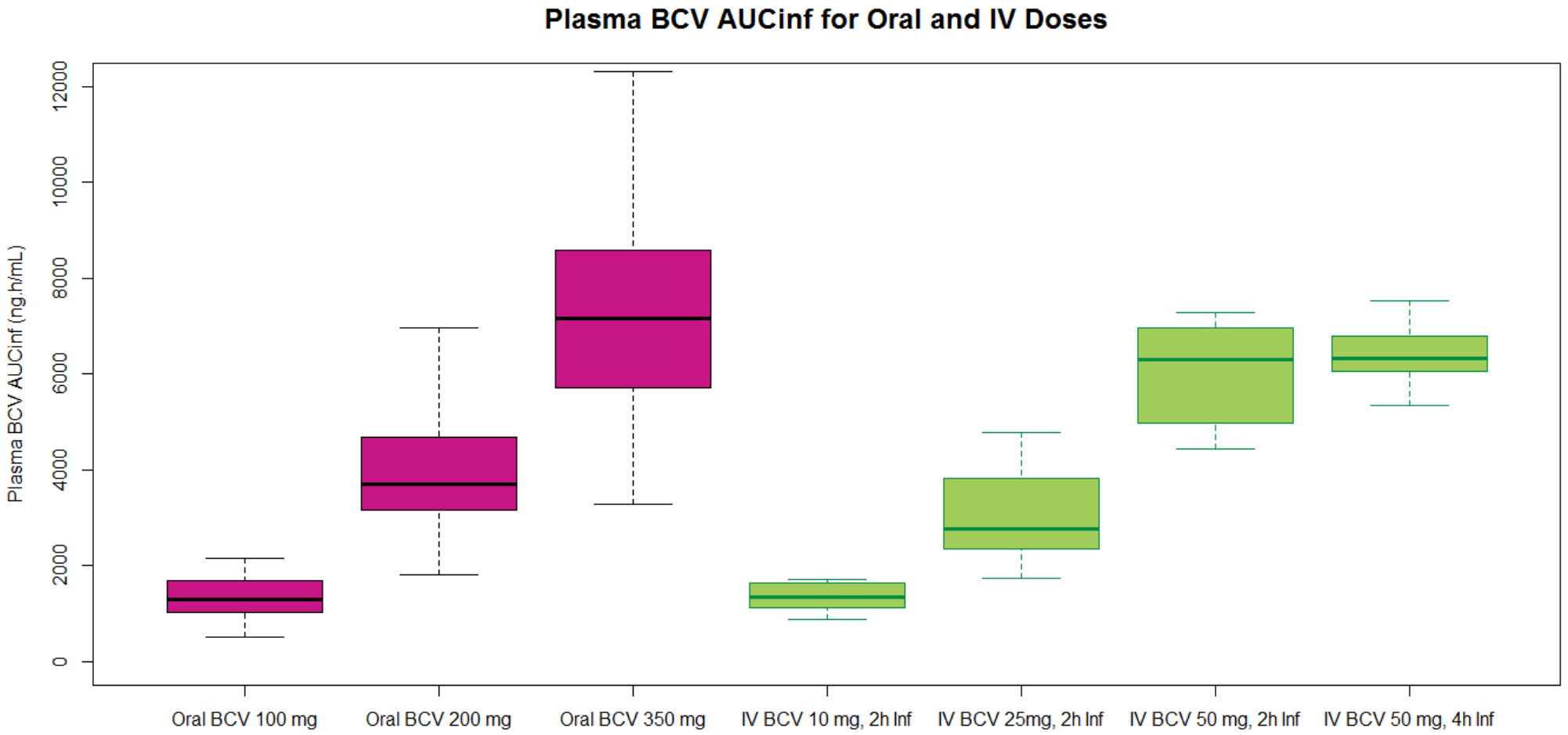
Plasma BCV AUC_{∞} Following IV and Oral Dosing: IV BCV 10 mg Achieved Exposure Equivalent to Oral BCV 100 mg



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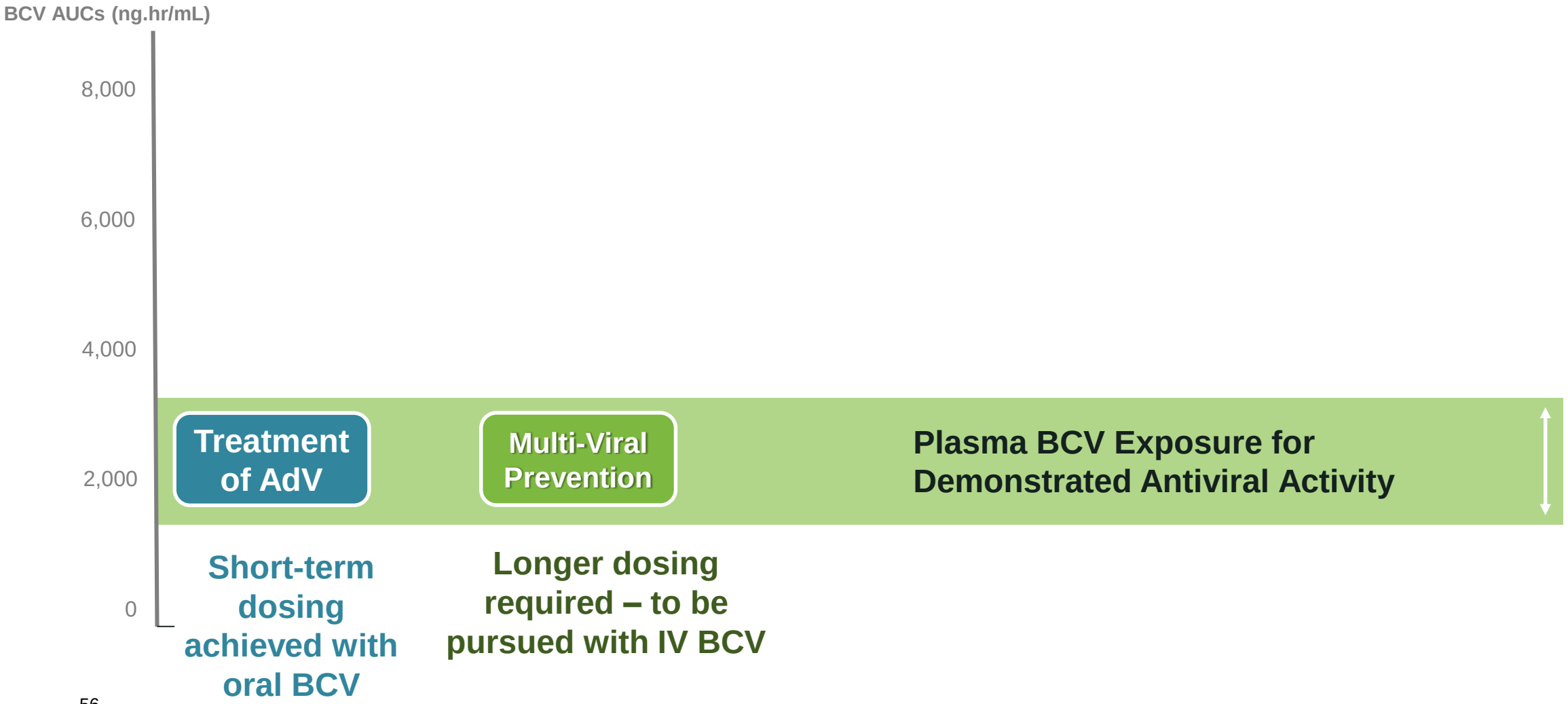
IV BCV 10-25 mg Provides Exposures Shown Efficacious for AdV Treatment and Viral Prevention



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Very Few Drug-Related AEs (All Grades) Observed With IV BCV

Subjects with AEs	Cohort 1 IV BCV 10 mg (2 hrs) n=6	Cohort 2 IV BCV 25 mg (2 hrs) n=6	Cohort 3 IV BCV 50 mg (2 hrs) n=9	Cohort 4 IV BCV 50 mg (4 hrs) n=9	Pooled Placebo n=10
	Therapeutic Doses		Supratherapeutic Doses		
Headache	0	0	2 (22%)	2 (22%)	0
Diarrhea	0	0	1 (11%)	3 (33%)	0
Nausea	0	0	0	2 (22%)	0
Decreased appetite	0	0	0	1 (11%)	0
Pain, phlebitis @ infusion site	0	0	1 (11%)	0	0
Elevated liver transaminases	0	0	0	1 (11%)	0

- In Cohort 3, 5 drug-related AEs in 4 subjects
- In Cohort 4, 9 drug-related AEs in 5 subjects

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No Grade 3/4 Drug-related AEs With Therapeutic Doses

Subjects with AEs	Cohort 1 IV BCV 10 mg (2 hrs) n=6	Cohort 2 IV BCV 25 mg (2 hrs) n=6	Cohort 3 IV BCV 50 mg (2 hrs) n=9	Cohort 4 IV BCV 50 mg (4 hrs) n=9	Pooled Placebo n=10
	Therapeutic Doses		Supratherapeutic Doses		
Headache	0	0	0	0	0
Diarrhea	0	0	0	0	0
Nausea	0	0	0	0	0
Decreased appetite	0	0	0	0	0
Pain, phlebitis @ infusion site	0	0	0	0	0
Elevated liver transaminases	0	0	0	1 (11%)	0

- No significant differences between placebo and IV BCV in other chemistries or hematologic parameters

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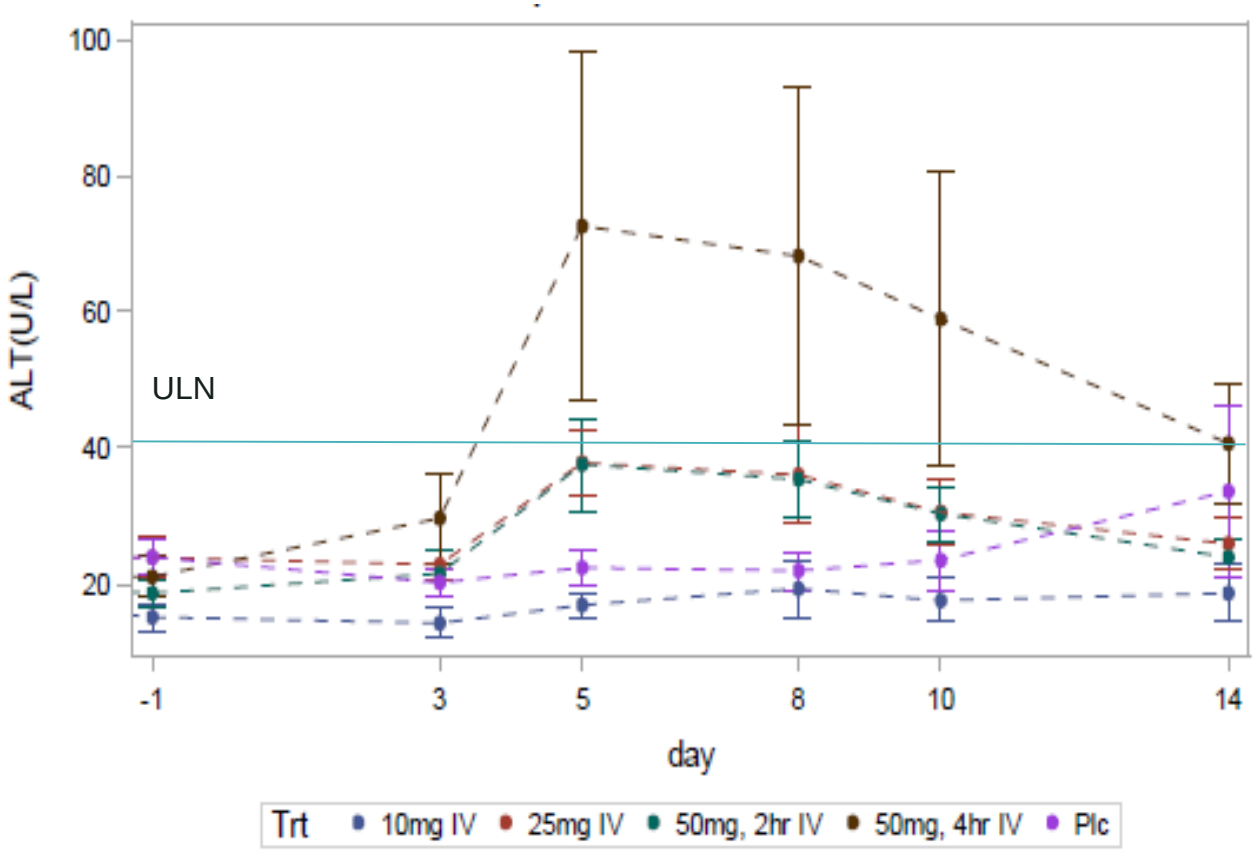
Dose-related, Reversible ALT Increase Observed with IV BCV

- In prior studies, oral BCV had reversible dose-related ALT increases in humans and preclinical species

<u>In IV BCV SAD Study</u>:

- At therapeutic IV exposures (Cohorts 1 & 2), no Grade 2 or higher ALT elevations
- At supratherapeutic exposures (Cohorts 3 & 4) transient Gr 2-3 ALT elevations noted in Cohort 4 only
- No Grade 2 or higher bilirubin in any cohort

Mean (+/- SE) ALT Levels Observed in IV BCV SAD Trial



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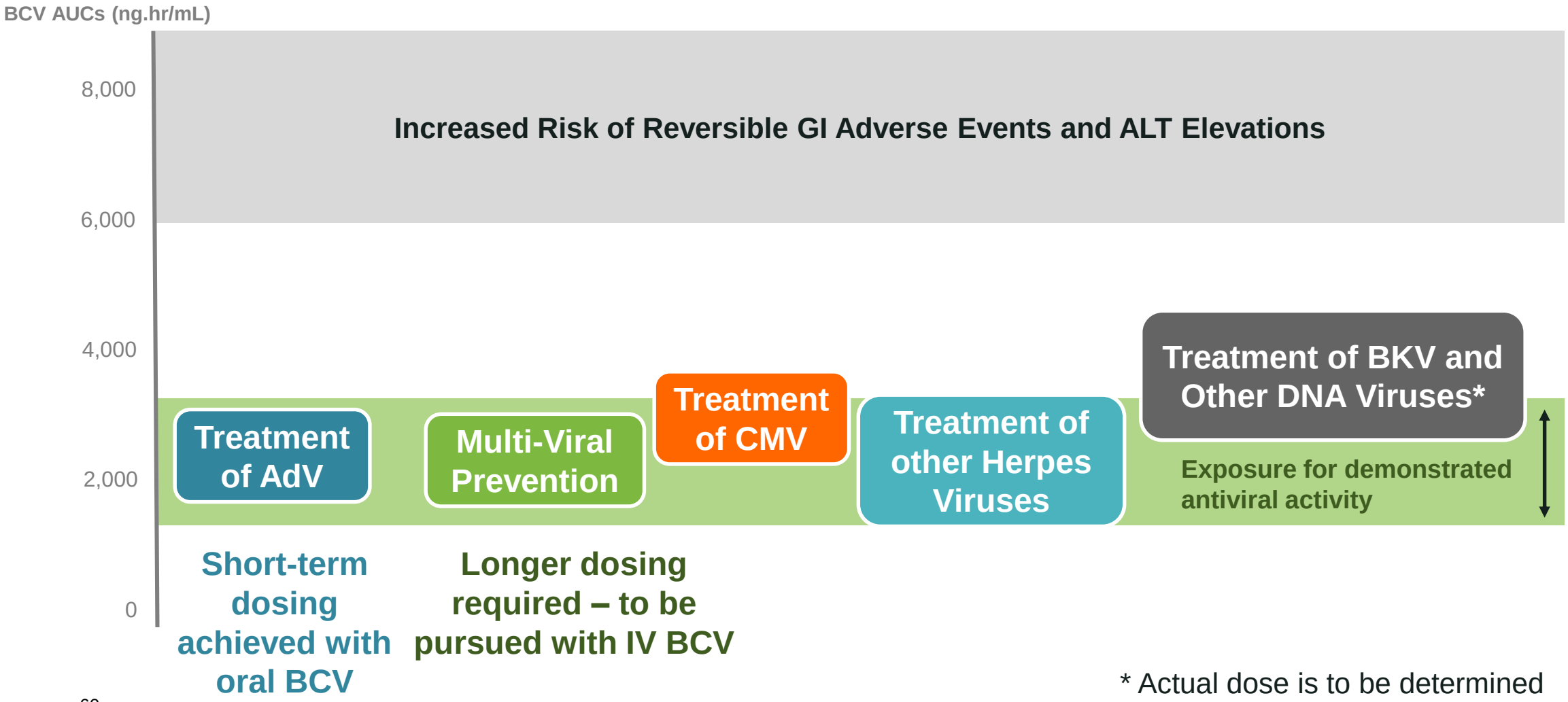
IV BCV May Allow Treatment and Prevention of Multiple DNA Viruses



* Actual dose is to be determined

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IV BCV Single Ascending Dose Study: Summary

- **IV BCV 10 mg provided plasma exposures comparable to oral BCV 100 mg, which showed antiviral effects in CMV prevention and Adenovirus treatment**
- **IV BCV provides exposures that may allow longer term dosing and thus provide treatment and prevention options for multiple DNA viral infections**

- Therapeutic doses (Cohorts 1 & 2, IV BCV 10 mg and 25 mg) were very well tolerated
  - No GI AEs reported – no other significant AEs or lab changes
- Supratherapeutic dose in Cohort 3 (50 mg given over 2 hours) was also well tolerated
  - Only 1 subject reported loose stools
- Supratherapeutic dose in Cohort 4 (50 mg given over 4 hours) achieved similar AUC, but appeared to be associated with higher rate of GI adverse events and ALT increases
  - Two hour infusion is both better tolerated and more convenient for patients

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Questions to Answer before Pivotal IV BCV Study

- What is safety/tolerability of multiple doses of IV BCV in healthy subjects?
- What is PK profile after multiple doses – is there accumulation?
  - Can weekly doses of IV BCV achieve adequate CDV-PP levels to treat and/or prevent DNA viral infections?
- Is PK profile similar in healthy subjects and virally infected patients?
  - Does IV BCV dosing based on weight yield similar exposures as suspension in children?
- What doses are associated with antiviral activity against CMV with and without evidence of viral resistance?

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IV BCV Multiple Dose Escalation Study Design

- Objectives:
  - Demonstrate safety/tolerability of multiple doses of IV BCV in healthy subjects with no background incidence of GI AEs
  - Demonstrate PK (including CDV-PP levels in PBMC) associated with multiple doses of IV BCV given weekly or twice weekly

Cohort	n Active/Placebo	Planned Doses
1	6 / 2	IV BCV 10 mg or placebo, QW (4 doses)
2	6 / 2	IV BCV 20 mg or placebo, QW (4 doses)
3	6 / 2	IV BCV 20 mg or placebo, BIW (4 doses)

Doses, time of infusion, and duration of treatment may vary during the study depending on PK, safety, and tolerability

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IV BCV Phase 2 Dose Range Finding Study in Adult Kidney Transplant Recipients with CMV Viremia

- Kidney transplant recipients do not typically have diarrhea with CMV reactivation
- Two part study – single dose followed by dose range-finding
- **Part 1 objective**: evaluate safety and PK of single dose IV BCV in kidney transplant recipients with CMV viremia
- **Part 2 objectives**:
  - Evaluate safety/PK/tolerability of multiple dose IV BCV given for 2-4 weeks
  - Determine optimal dose for pre-emptive treatment of CMV (vs. valganciclovir, VGCV)

Doses, time of infusion, and duration of treatment may be adjusted depending on PK, safety, and tolerability from Part 1 of the study

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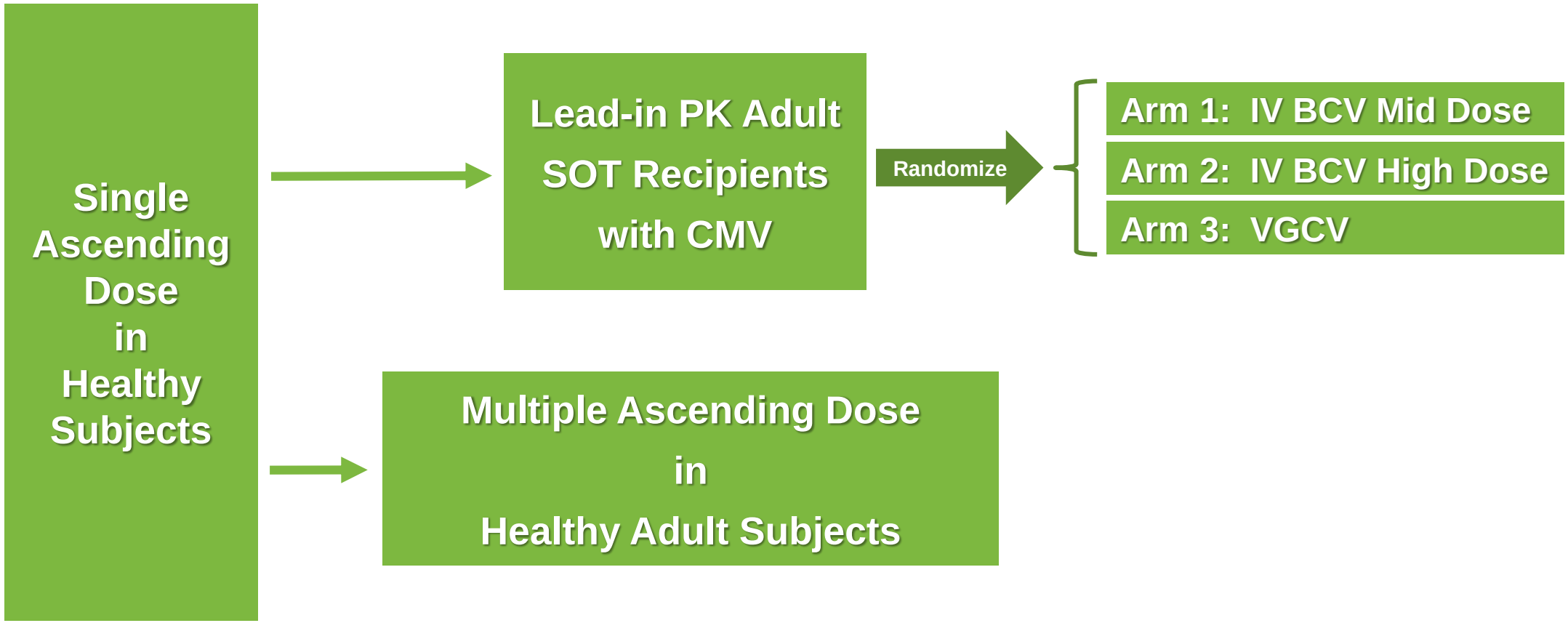
IV BCV Dose Range Finding Trial Designs



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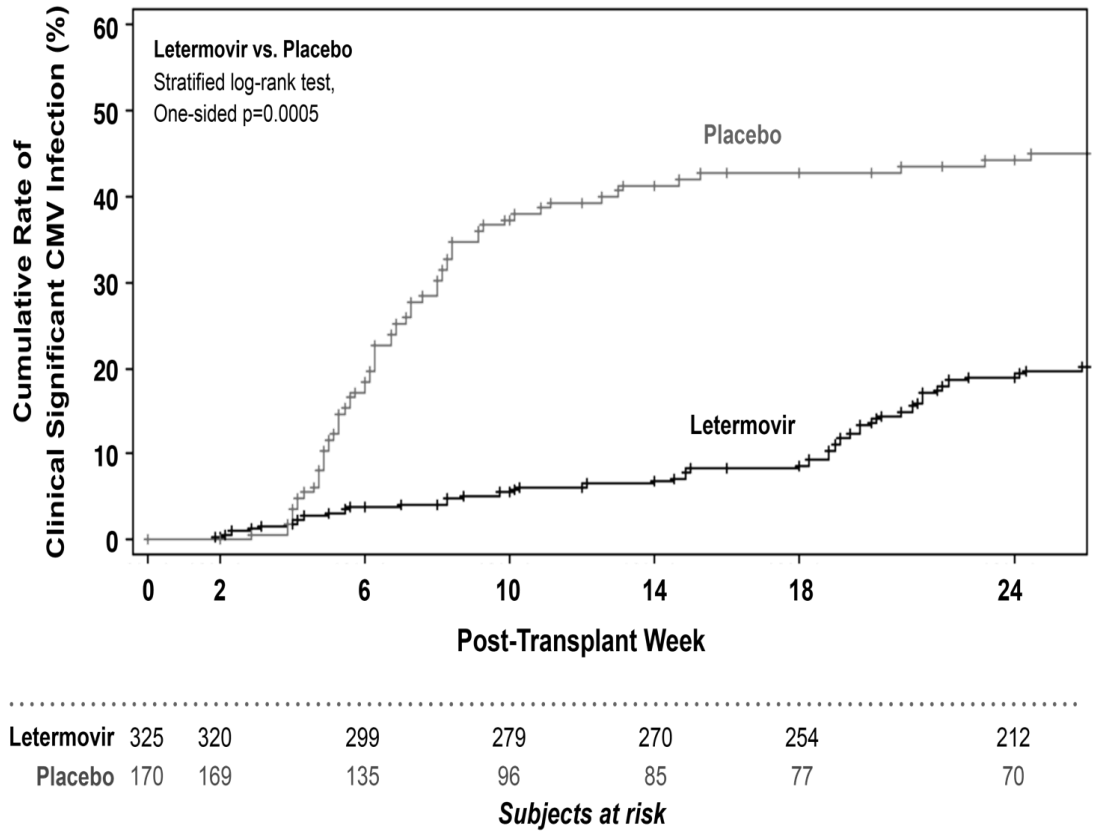
Competitive Landscape: Letermovir

- Letermovir met primary endpoint for CMV prophylaxis
  - Follow-up continuing to Week 48
- Letermovir gaps:
  - Prophylaxis only: with low barrier to resistance, not currently being pursued as treatment for active CMV infection
  - Adult data only
  - CMV only:
    - Acyclovir must be used to cover herpes simplex and varicella zoster viruses
    - No activity against other DNA viruses that affect transplant patients

Figure 1. Time to Onset of Clinically Significant CMV Infection

Subjects with undetectable CMV DNA at Randomization



Marty F et al. Tandem BMT 2017, Orlando, FL

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IV BCV: Options for Pivotal Trial for Multi-Viral Prevention

- What is primary endpoint - prevention of CMV or AdV?
  - CMV: if letermovir serves as the control, must await commercial letermovir availability, followed by time to produce matched placebo – trial delayed until 2019
  - AdV: no approved therapy, high unmet need

- What is our population (adult or pediatric allogeneic HCT)?
  - Pediatric patients more commonly reactivate adenovirus in addition to multiple DNA viruses

- Superiority vs placebo OR non-inferiority vs active control
  - Non-inferiority vs. letermovir would be larger than placebo control
  - Placebo control is preferred – smaller study, clinical supplies may be created now

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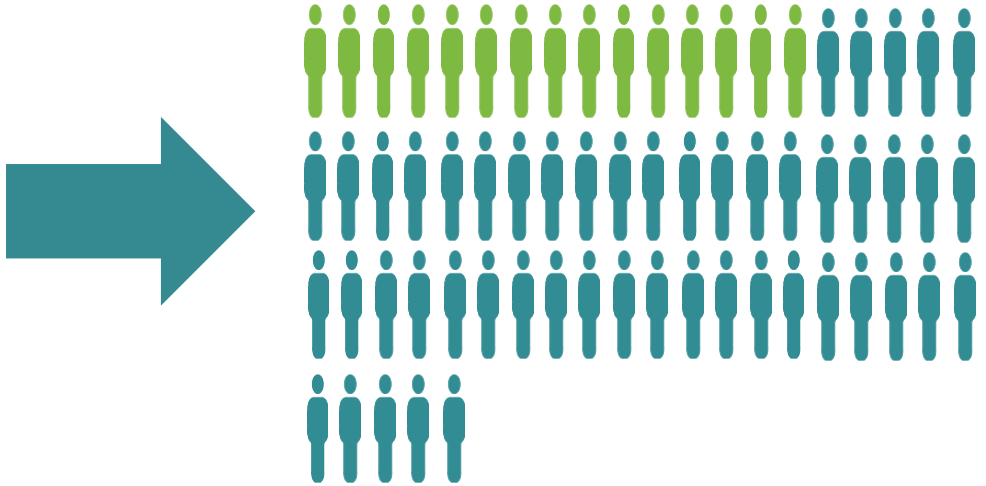
Adult and Pediatric HCT Recipients Face Risks Beyond CMV

- Of the HCT recipients who reactivated CMV, **>75% had at least one other DNA virus identified** and were at increased risk of mortality



- 1 in 3 HCT recipients had ≥3 DNA viral infections detected
- Pediatric Allo-HCT recipients commonly reactivate AdV, BKV, HHV-6 early after transplant

More DNA viruses reactivating = higher risk of death

Hill JA et al. Blood. 2017 Feb 16. pii: blood-2016-10-748426. doi: 10.1182/blood-2016-10-748426. [Epub ahead of print] 400+ HCT Recipients at Fred Hutchison Cancer Research Center

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Demonstrating IV Brinci's Multi-Viral Prevention: MVP-Peds

- 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
- Proposal: **placebo-controlled trial of IV BCV in pediatric allogeneic HCT recipients**
  - Primary endpoint of prevention of adenovirus 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 other DNA virus prevention and health outcomes
- Benefits:
  - Superiority design allows smaller study than head-to-head non-inferiority trial for CMV vs letermovir

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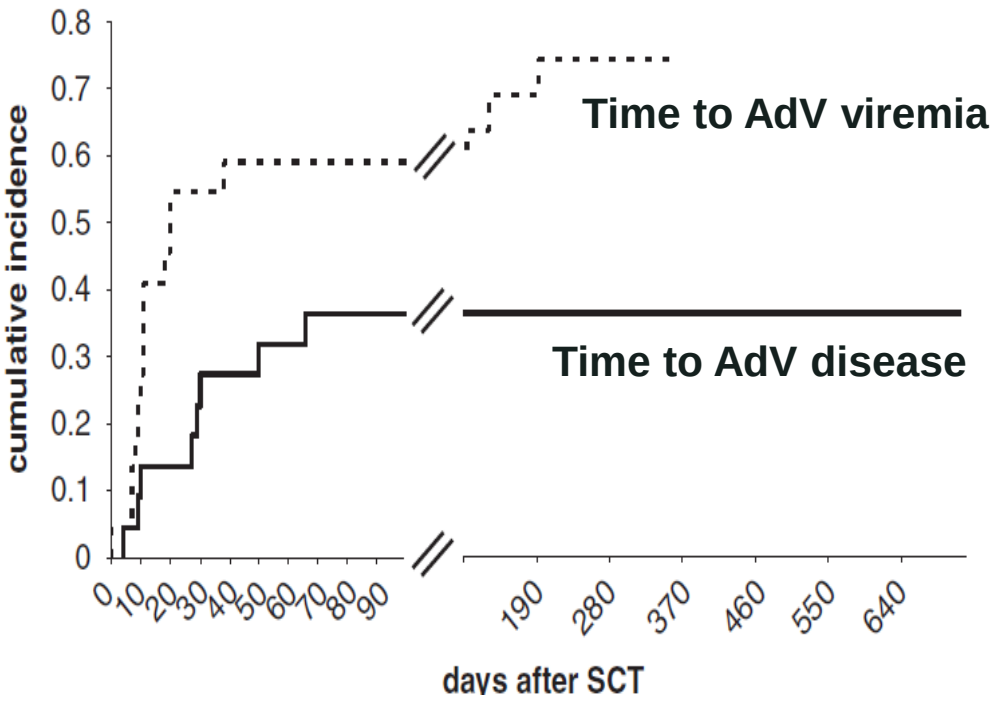
IV BCV: Selecting an Enriched Population for MVP-Peds

- Pediatric allo-HCT recipients with shedding of AdV in stool >10^6 AdV copies/g predicts high risk of AdV viremia and AdV disease
- Pediatric HCT recipients with positive stool AdV have:
  - **59%** incidence of AdV viremia in 1st 100 days
  - **36%** incidence of disseminated AdV disease
- Ph 2/3 PBO-controlled study proposal
  - **Primary endpoint: AdV disease**



Time to viremia (dashed line) and disseminated AdV disease (solid line) in patients with high AdV load in stool

Lion T et al. Leukemia 2010;24:706–714

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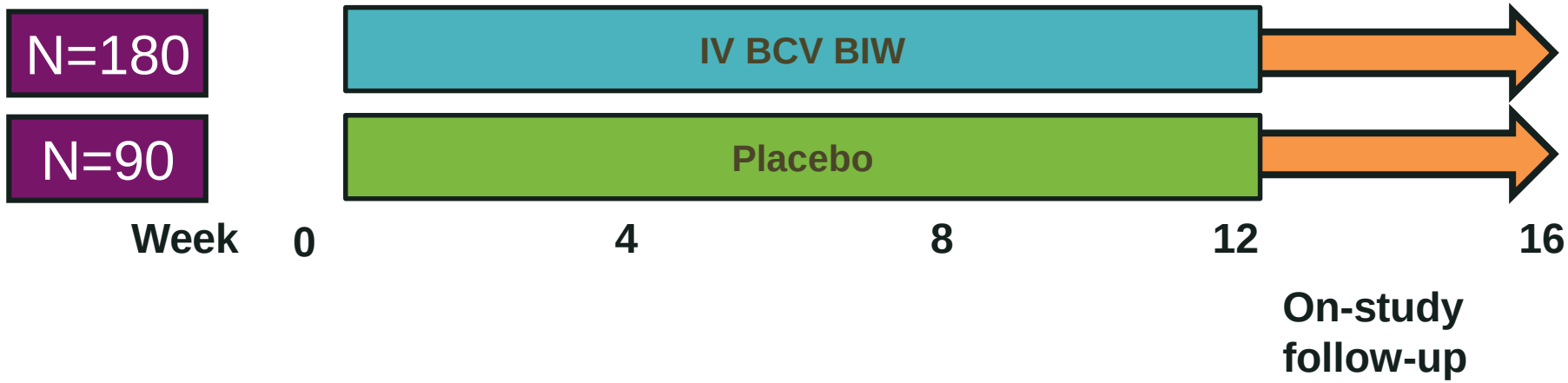
MVP-Peds:
IV BCV for Prevention of AdV and other DNA Viruses After HCT

- Randomized, double-blind trial of IV BCV vs. placebo
  - Population: pediatric allo-HCT with > 10^6 c/g AdV DNA in stool, <100 days from HCT
- **Primary endpoint: proportion with AdV disease** through week 16 after transplant
  - N~270 (2:1, 85% power) for reduction in AdV disease from 36% to 18%
- **Secondary endpoint: CMV reactivation** requiring preemptive therapy (SUPPRESS endpoint) and other DNA viruses



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IV Brinci for Multi-Viral Prevention (MVP-Peds): Conclusions

- With no approved therapies for adenovirus, a pediatric study that targets prevention of AdV disease represents most efficient regulatory pathway for IV BCV
  - This population can be enriched (e.g., by screening for AdV in stool) to enhance differences between active and placebo arms

- Pediatric patients often reactivate multiple DNA viruses after HCT
  - Inclusion of secondary endpoints (CMV reactivation requiring preemptive therapy, BKV-associated hemorrhagic cystitis) can build value story and provide proof-of-concept for multiviral prevention in other populations not studied

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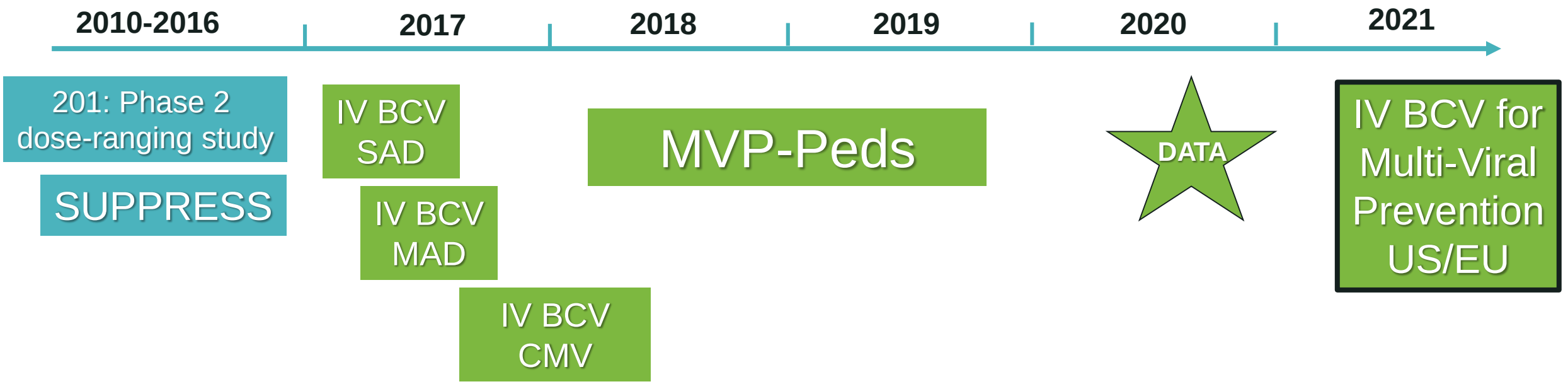
IV Brincidofovir for Multi-Viral Prevention in HCT Recipients: Development and Approval Timelines



- MVP-Peds provides the opportunity to demonstrate the importance of preventing multiple DNA viral infections in a placebo-controlled superiority pivotal study
- Dosing of IV BCV in adults will be established in treatment settings

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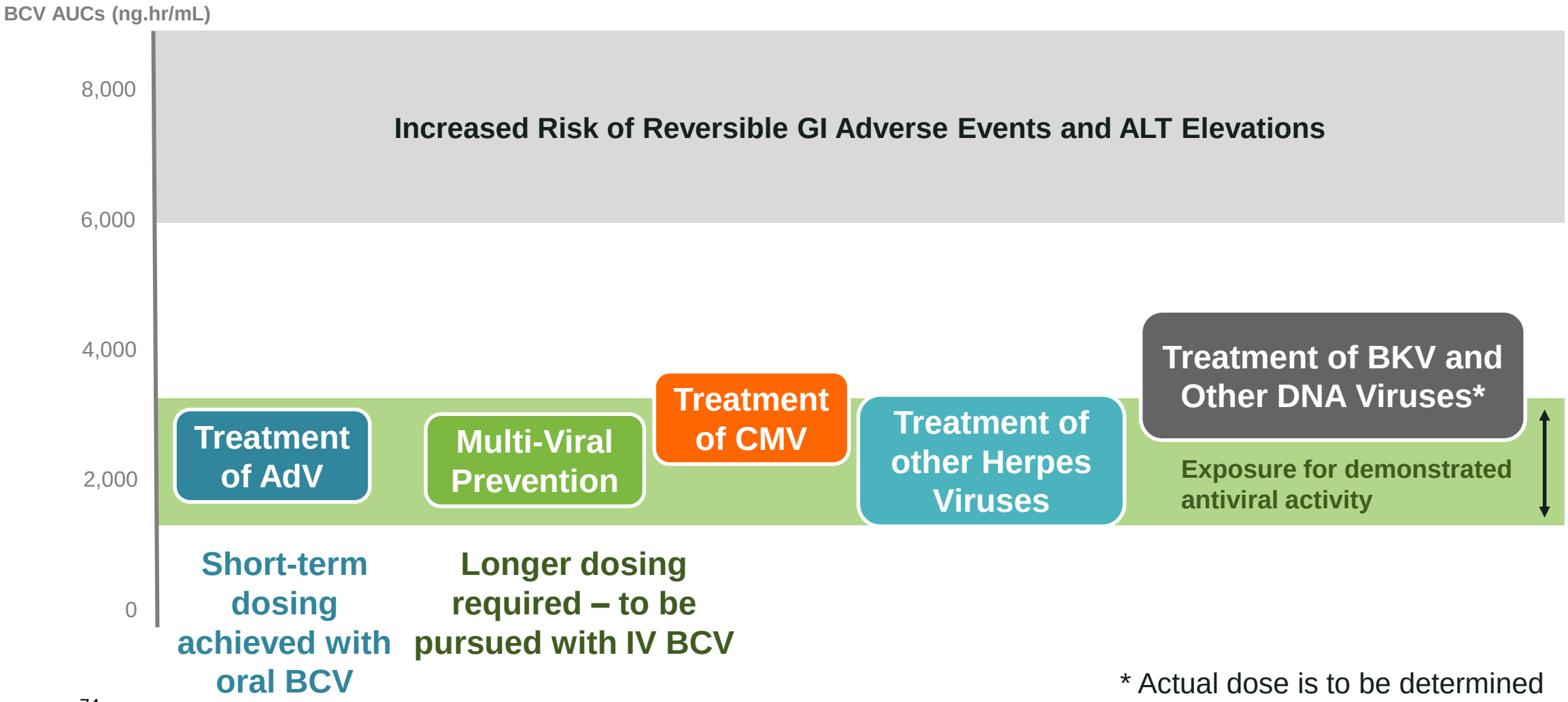
IV BCV May Support Treatment of Multiple Viral Infections in HCT/SOT Recipients and Other Patient Populations



* Actual dose is to be determined

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“LAND & EXPAND” – LAUNCH STRATEGY AND THE MARKET OPPORTUNITY FOR BRINCIDOFOVIR

Linda M. Richardson

Chief Strategy and Commercial Officer

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Overview

- There is a significant commercial opportunity for brincidofovir
  - desirable core product attributes and potential benefits
  - a high degree of unmet need in a variety of patient populations
  - lack of near or mid-term competitive therapies against many of the DNA viruses
  - expanding recognition and diagnosis of AdV infections in non-transplant populations
  - significant benefits from Orphan Drug designation
  - patent protection until 2034
- “Land and Expand” strategy results in potential significant upside beyond AdV launch indication

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Background Information

- There are no approved therapies for the treatment or prevention of AdV infections
  - T-Cell therapies in development are likely to be limited in use to allogeneic HCT recipients
    - Available data suggest benefits are limited to resolving viremia, did not improve clinical signs/symptoms of end-organ disease
- Current options to manage AdV infections often provide suboptimal results
- Demand for oral brinci via Named Patient Programs and Study 351 remains strong
- Brinci has demonstrated strong antiviral activity against a variety of DNA viruses
- Growing awareness that transplant population is at risk for more than CMV infection
  - Impact of multiple infections leads to additional morbidity and mortality risks

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Potential Benefits of Orphan Drug Status

- No requirement for head-to-head study vs a competitor in AdV in EU
- Supplemental funds are available for coverage in several EU markets
- European and US pricing has remained comparable for orphan medicines
- Evaluate Pharma, Inc. reports have characterized Orphan Drug Costs in the US over the past few years (based on top 100 drugs)
  - 2014: Average cost per patient per year: $138K Median: $89K
  - 2015: Average cost per patient per year: $140K Median: $80K
  - **2016: Average cost per patient per year: $140K Median: $84K**

Orphan Drug Report 2017. Evaluate Pharma (Feb 2017)

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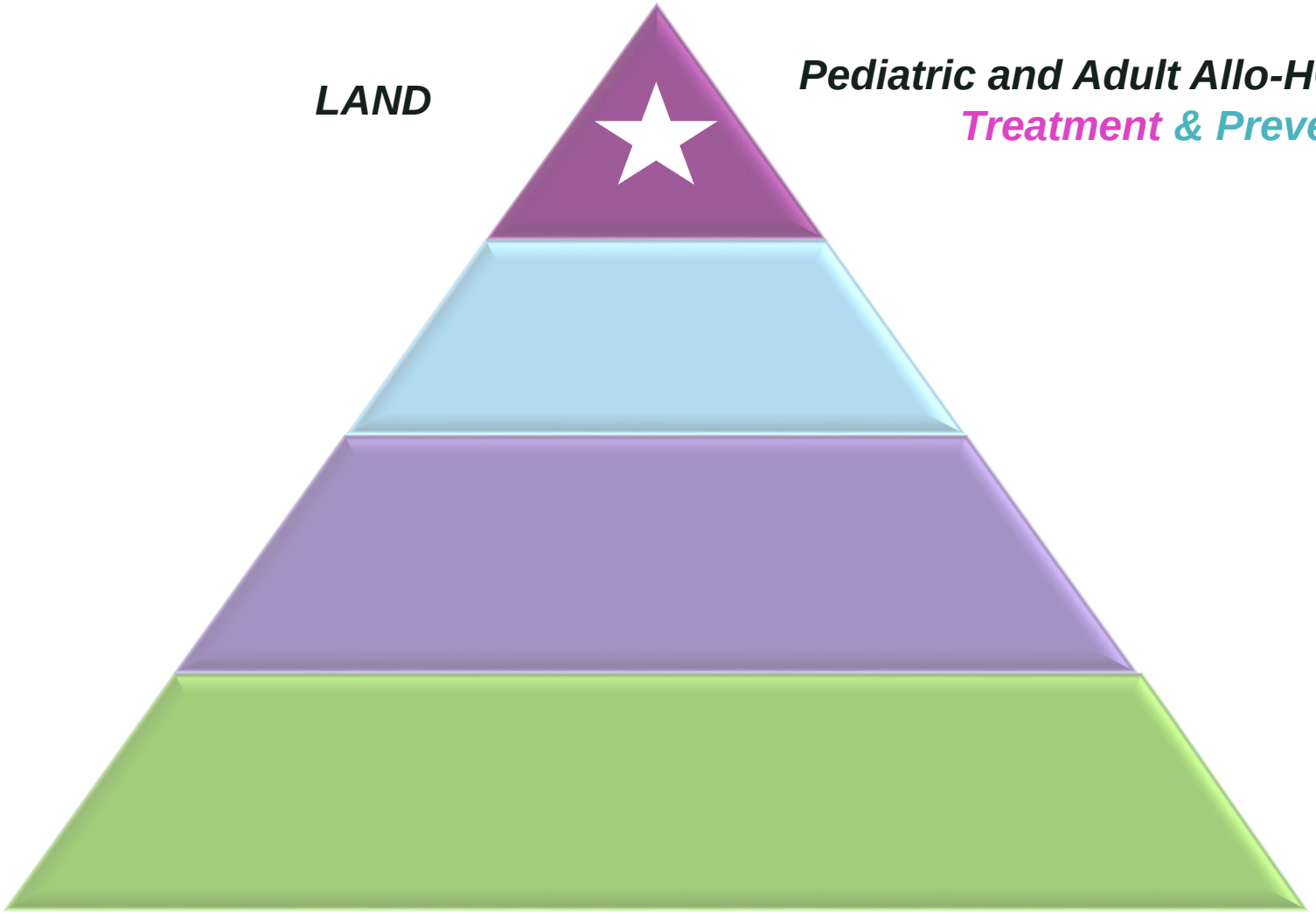
Building Value for Brincidofovir – “Land and Expand”



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Opportunities in the Growing Transplant Market

TRANSPLANTS PER YEAR	US	EU
HCT :		
Allogeneic	**8,500 (38%)**	**16,000 (42%)**
• *Adults*	*7,000 (82%)*	*12,800 (80%)*
• *Peds*	*1,500 (18%)*	*3,200 (20%)*
Autologous	**13,700 (62%)**	**22,100 (58%)**
• *Adults*	*12,700 (92%)*	*21,000 (95%)*
• *Peds*	*1,000 (8%)*	*1,100 (5%)*
HCT TOTALS	**22,200**	**38,100**
SOT :		
Kidney	**18,600**	**20,000**
• *Adults*	*17,900 (96%)*	*19,500 (98%)*
• *Peds*	*700 (4%)*	*500 (2%)*
Liver	**7,100**	**7,400**
• *Adults*	*6,500 (92%)*	*6,900 (93%)*
• *Peds*	*600 (8%)*	*500 (7%)*
Other SOT	**5,200**	**4,500**
• *Adults*	*4,600 (89%)*	*4,300 (96%)*
• *Peds*	*600 (11%)*	*200 (4%)*
SOT TOTALS	**30,900**	**31,900**
GRAND TOTALS	**53,100**	**70,000**

- US HCT: 2014 figures from CIBMTR. Auto transplants are increased by 20% to account for under-reporting to CIBMTR.
- US SOT: 2015 figures from Organ Procurement and Transplantation Network (OPTN).
- EU HCT: JR Passweg, et al., HSCT in Europe 2014, nature.com/bmt, 2016. Analysis included a total of 49 countries, data from 9 non-EU countries has been removed. Adult vs ped HCT break-out is estimated based on data available in the paper.
- EU SOT: Newsletter Transplant – International Figures On Donation And Transplantation 2014; EDQM, volume 20, 2015. includes 28 EU countries, pediatric patients <15 years of age

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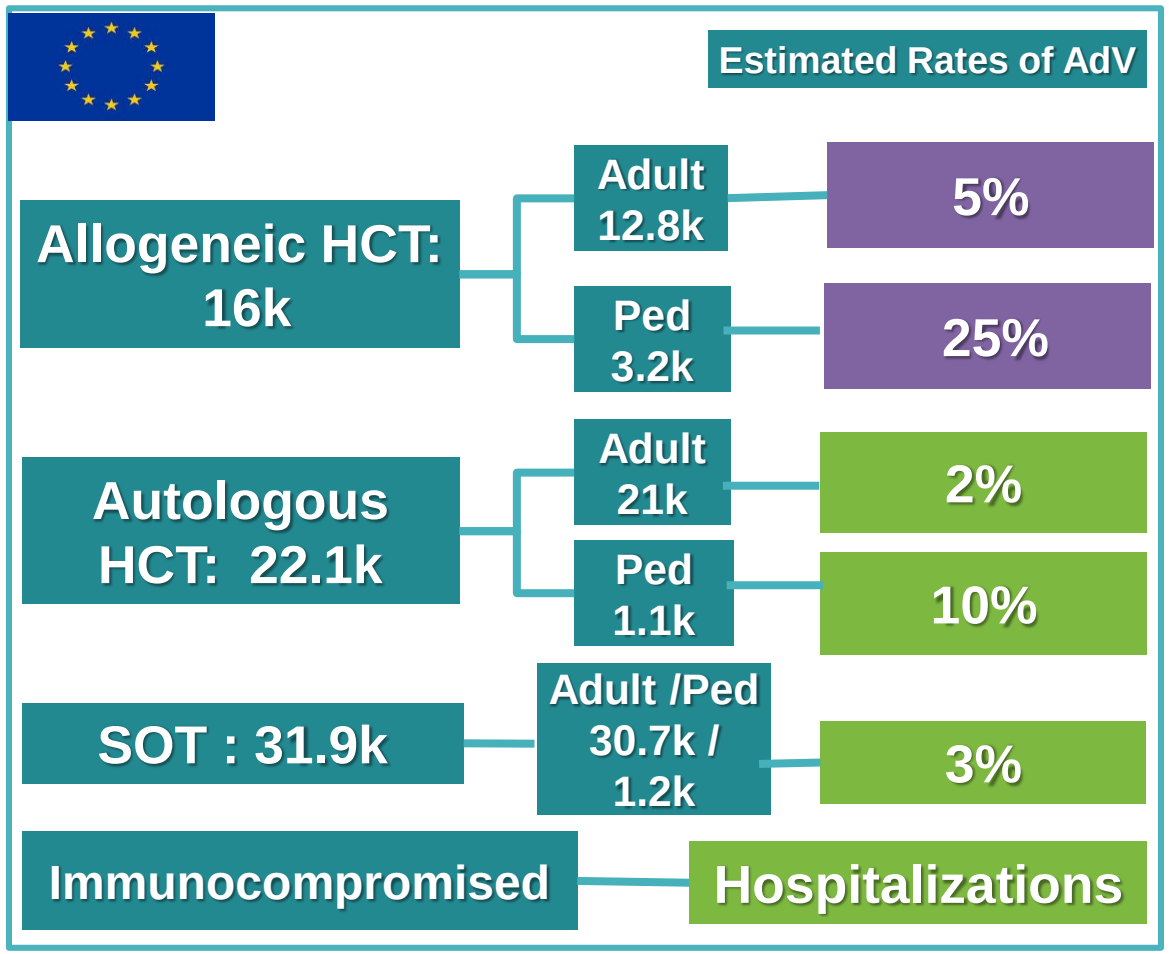
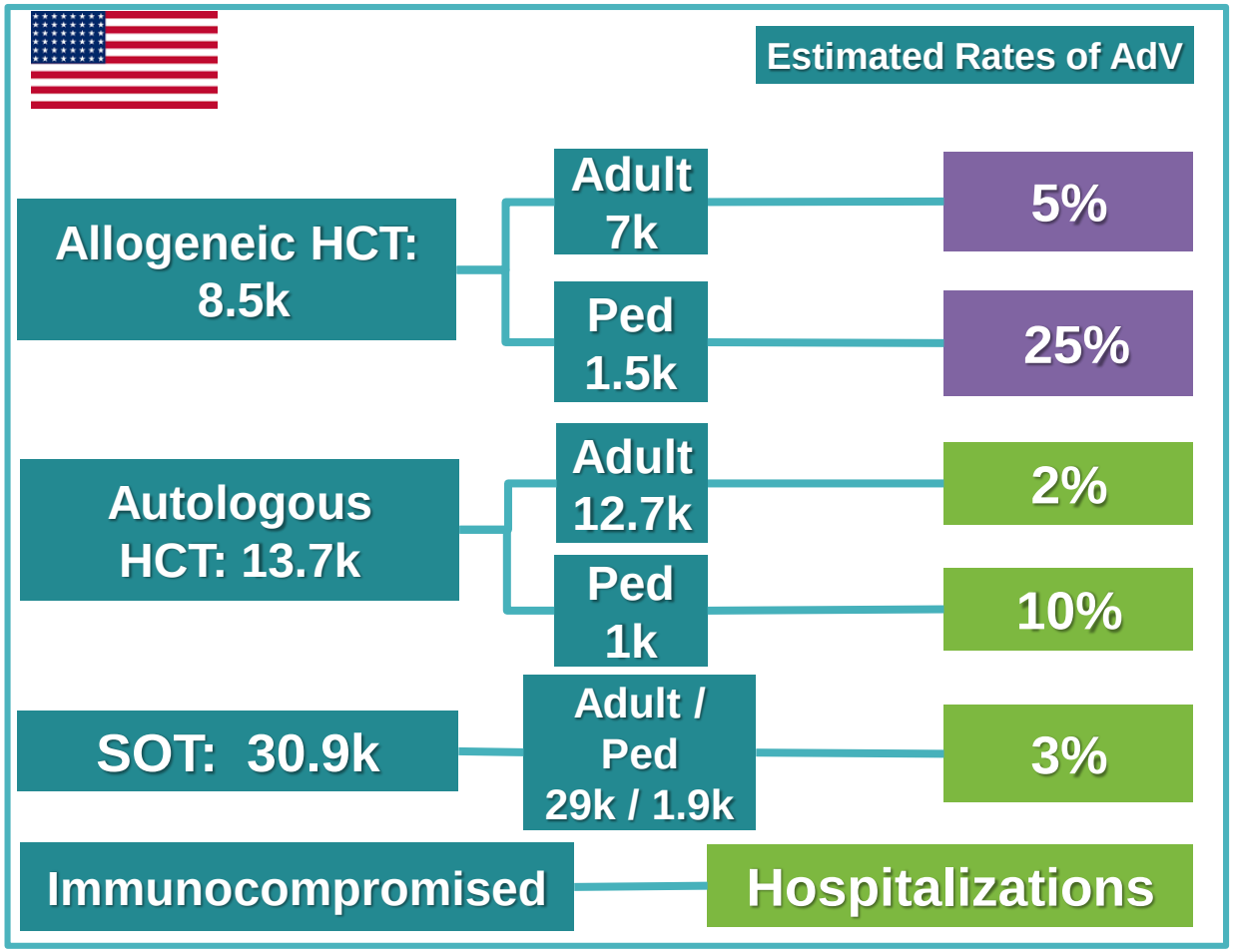
Earlier screening and diagnosis of AdV in prevention would likely increase the estimated rates of infection in Allo-HCT





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Healthcare Cost and Utilization Project's (HCUP) National Inpatient Sample (NIS) – AdV-related Hospitalizations

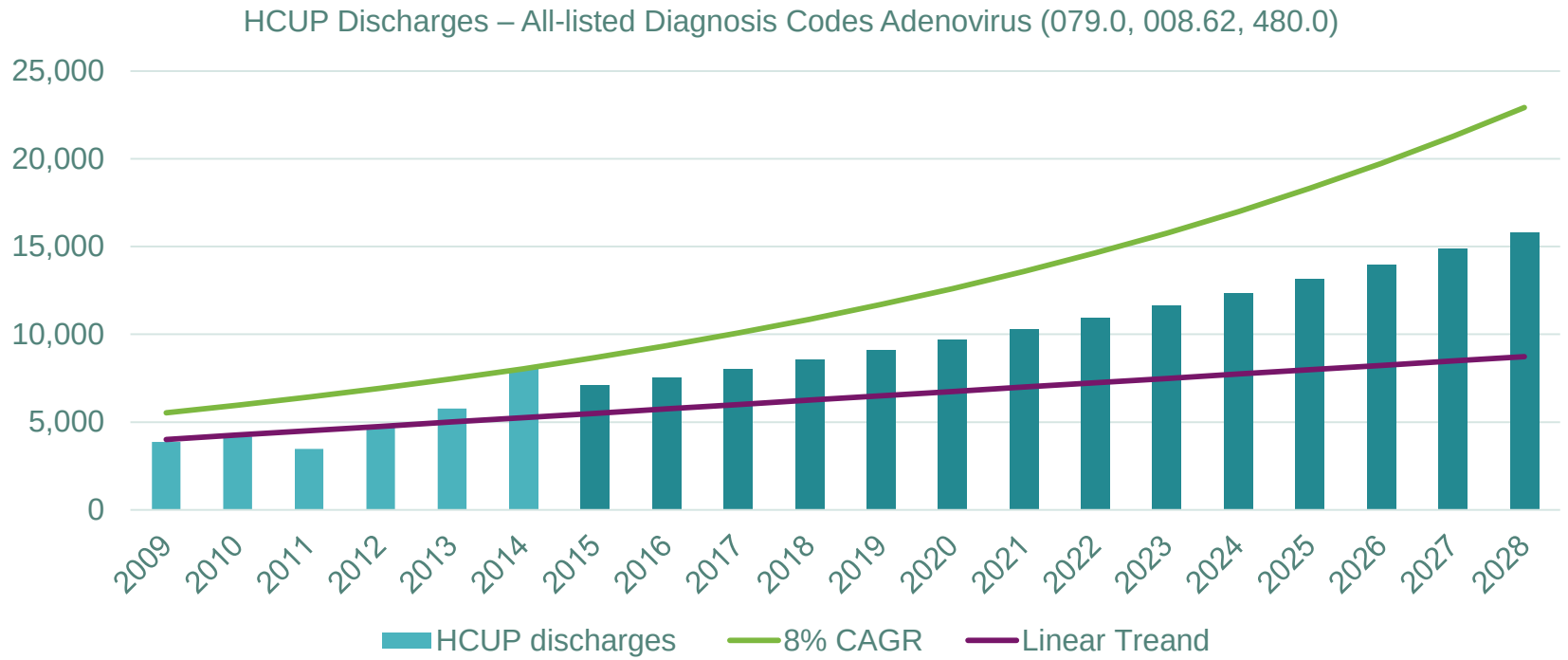
- HCUP includes the largest collection of publically available hospital care data
- National Inpatient Sample (NIS) is one of the HCUP databases
  - largest all-payer inpatient database in the US, containing discharge-level information
  - a 20% sample (>7MM/year) of discharges from all community hospitals participating in HCUP
    - Weighted, HCUP estimates more than 35 million hospitalizations nationally
- Researchers and policymakers use NIS data to identify, track, analyze and compare hospital statistics at the national level
- AdV-related hospitalizations using ICD-9 codes:
  - 079.0 (AdV infections NOS), 008.62 (intestinal infection due to AdV), 480.0 (AdV pneumonia)

Source: http://www.hcup-us.ahrq.gov

BCV: An Opportunity For Treatment of AdV Infections Beyond Transplant

Nearly 8000 Hospitalizations Annually

U.S. AdV-Related Hospital Discharges: 2009-2014 Actual, Trended From 2015



- In addition to stem cell and organ transplant recipients, other at-risk populations include newborns with severe combined immunodeficiency (SCID), individuals on chemotherapy or biologics for autoimmune diseases, and other immune deficiencies

Source: HCUP database (4-19-17) – historical CAGR (1993-2014) is ~8%, linear trend is ~5%, trended HCUP discharges are ~6% (average of CAGR + linear trend)

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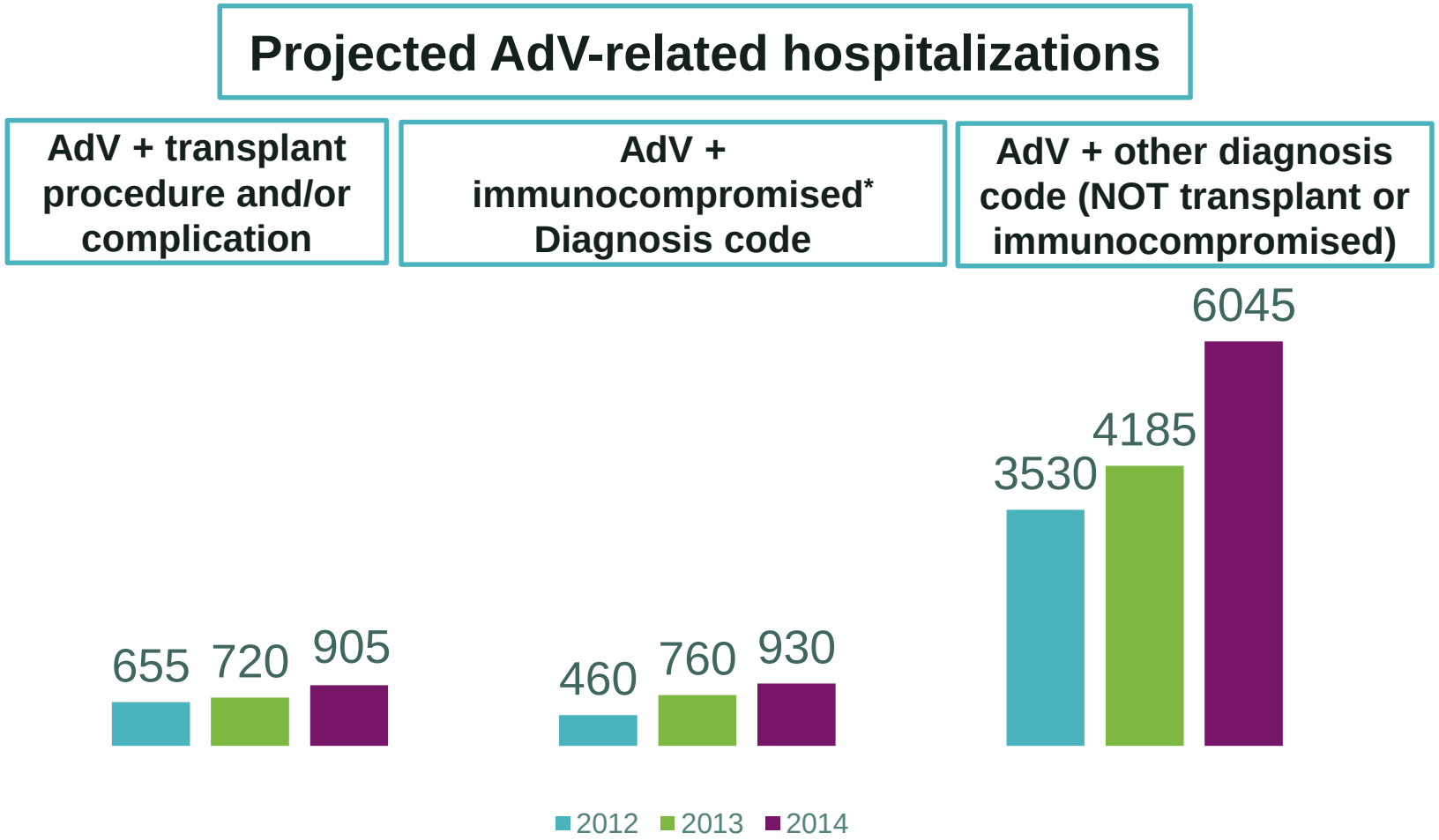
Most U.S. AdV-related Hospitalizations are NOT in Transplant Recipients or Immunocompromised Patients



*AdV+immunocompromised excludes 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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Identifying the Future Opportunity in AdV Infections

- Patient Characteristics:
  - Admitted to major teaching hospitals and diagnosed with AdV
  - Immunocompromised patients are at risk for opportunistic infections
    - Patients on biologics
    - Oncology patients - particularly lymphoma, leukemia
  - Patients with chronic underlying heart or respiratory conditions, Cystic Fibrosis
- Increase in multiplex PCR screening? Greater awareness of AdV?
- Are they candidates for treatment?
  - Risk-benefit profile of brinci will factor in to decisions
- Can we reach the prescriber base? Infectious Disease? ER? Pulmonologists?
  - Will need to identify educational and clinical support to pursue market expansion in appropriate patient and healthcare provider segments

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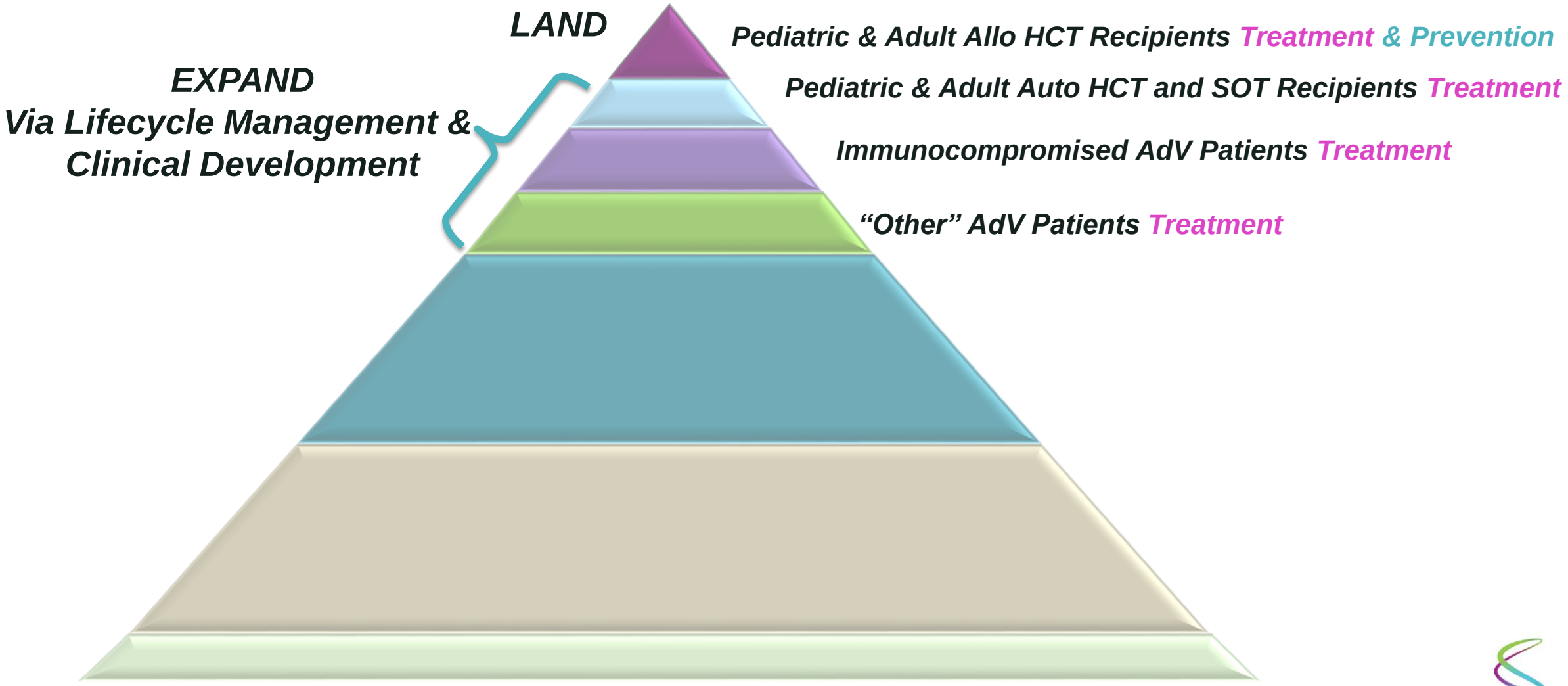
Building Full Potential Value in *Adenovirus* for BCV "Land and Expand"



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Competitiveness of Brincidofovir in the Transplant Setting

- Significant portion of the allo-HCT population is at high risk for reactivating CMV
  - These patients are also susceptible to other DNA viral infections
  - Higher risk of significant morbidity, mortality and healthcare utilization

- What will healthcare providers do to prevent or treat these other infections, if a therapy becomes available that has demonstrated activity against CMV, AdV, BKV and other viral threats?

- What level of evidence will pharmacy directors and payers require to evaluate their options?

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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
  - 16% of kidney transplant recipients develop BKV viremia in the first year post-transplant
- Key area of clinical development for IV BCV program

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

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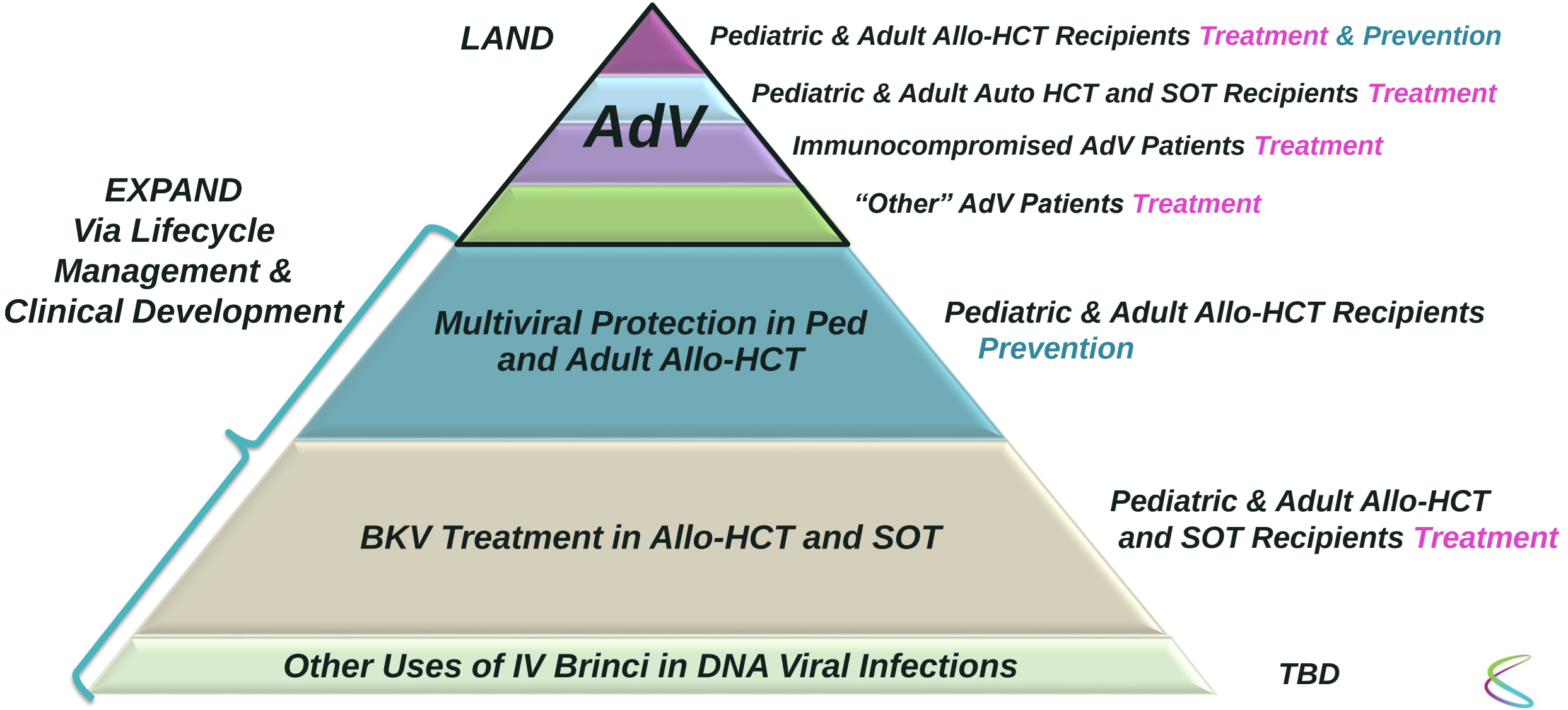
Building Full Potential Value for BCV – "Land and Expand"



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“Land and Expand” Strategy

- **Land**: Establish the beach-head in pediatric Allo-HCT recipients with AdV in AdAPT
  - Expand understanding of AdV infections in non-transplant patients
- **Expand:** Demonstrate Multi-Viral Prevention with IV BCV in pediatric patients in MVP-Peds
  - Educate HCPs and payers on the impact and costs of multiple viral infections in at-risk patient populations
- **Expand:** Conduct label-informing and indication studies in CMV and BKV treatment
  - HCT and Solid Organ Transplant Recipients

GOAL: Establish brincidofovir as the potential single solution for multiple infections through robust clinical development and commercialization programs

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CHIMERIX 2020-2025

M. Michelle Berrey, MD, MPH
President and CEO

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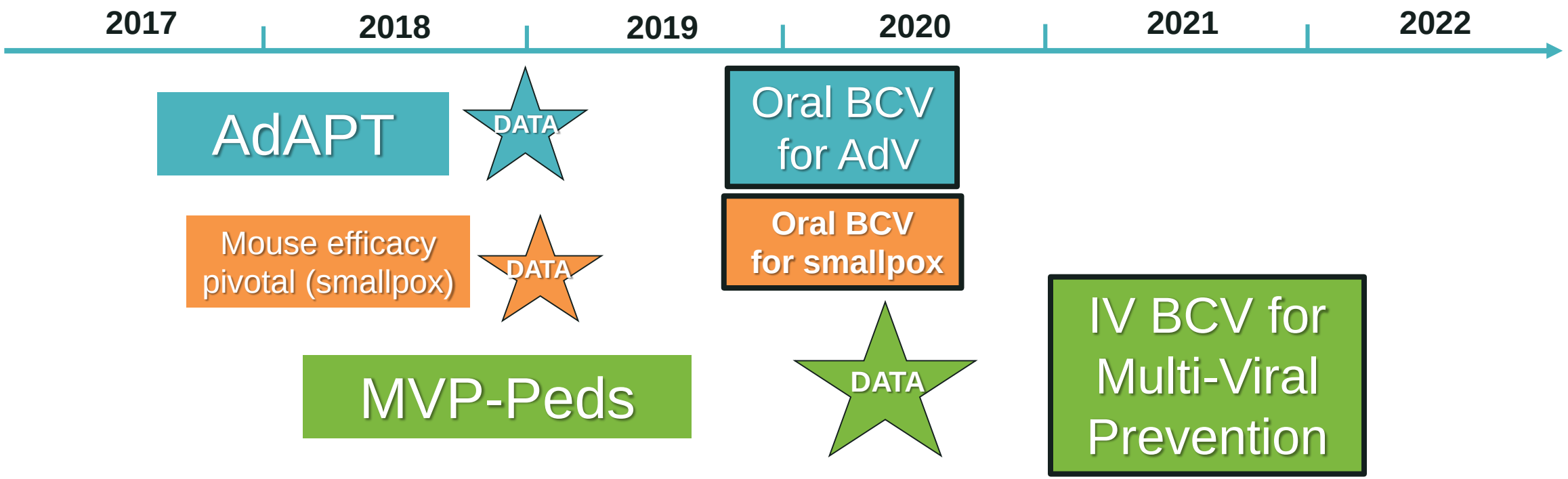
IV Brincidofovir for Multi-Viral Prevention in HCT Recipients: Development and Approval Timelines



- AdAPT: oral BCV for short-course treatment of AdV
- Smallpox: Final mouse pivotal in final discussions for conduct in 2017
- MVP-Peds: IV BCV to prevent multiple DNA viral infections in high-risk HCT

All timelines are estimated

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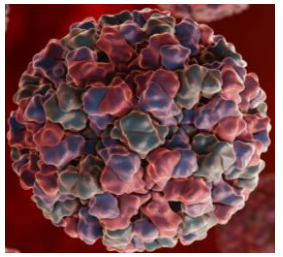
Norovirus: CMX521 On Track



- Unmet Need/Opportunity
  - Acute prophylaxis: ~ 20 million cases/year; most reported outbreaks (>60%) are in health care facilities
  - Treatment: chronic norovirus infection may occur in 15-20% of HCT and SOT; associated with chronic, severe diarrhea & graft rejection
- CMX521
  - IND and FTIH on-track for 2H 2017
  - Clinical Trial Material for Phase 1 studies is manufactured and on stability
- Early 2018:
  - Clinical development plan including challenge study (POC) and safety database
  - Target product profiles for treatment and prevention
  - Current and planned market research and commercial analysis/preparations

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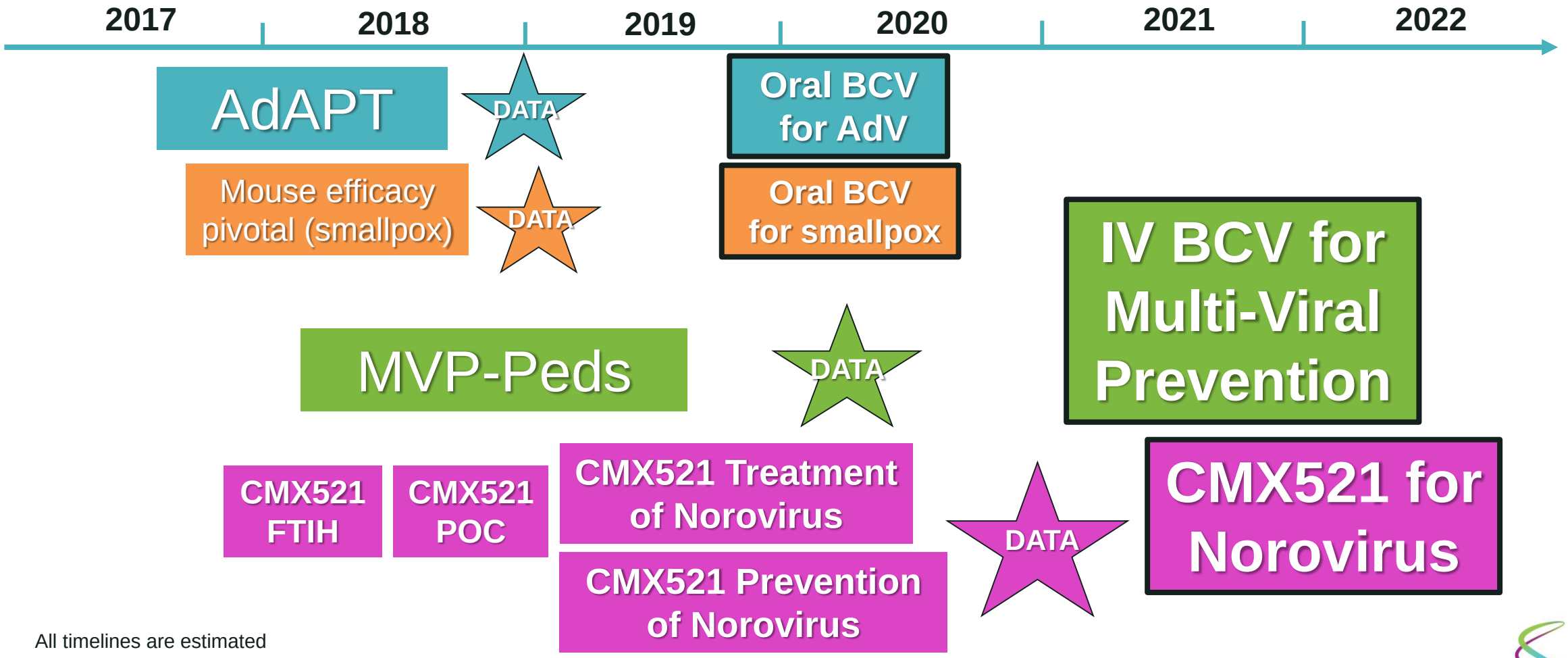
Chimerix Continues to Build Out Our Pipeline With Solutions for Patients at Risk of Serious Viral Infections



All timelines are estimated

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Chimerix Pipeline

	Program	Discovery	Pre-clinical	Phase 1	Phase 2	Phase 3	Anticipated Approval
Short-course Oral BCV	AdV Treatment	AdAPT in EU (+/- US) to start in 2H 2017					2020
	Smallpox	Data from second animal efficacy model in 2017					2019
IV BCV	Multi-viral Prevention	Data from MAD in 2017			Ph 2/3 MVP-Peds HCT		2021
	CMV Treatment	Initiate Dosing late 2017					
	BKV Treatment	Initiate Dosing 2018			Ph 2/3 in Kidney Tx		2023
CMX521	Norovirus	IND 2H 2017		FTIH & POC	Prevention Field Testing & Treatment Ph 3		2022
CMX157	HBV Treatment	*Licensed to ContraVir					

All timelines are estimated
* Development per ContraVir's website

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