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DEDICATED TO PREVENTING AND TREATING LIFE-THREATENING VIRAL INFECTIONS

February 22, 2016

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 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 Quarterly Report on Form 10-Q for the quarter ended September 30, 2015, as filed with 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.

Discovering, Developing and Commercializing Life-Saving Therapies

- Prevention and treatment of **CMV** and other **DNA viruses (BKV, HHV-6, EBV)** common in high-risk patient populations
  - Prevention and treatment of **CMV** in high-risk patient populations
  - Prevention and treatment of serious **adenovirus** (AdV) infections in pediatric and adult patients
  - Treatment of **smallpox** in the event of a bioweapon event
  - Adjunct treatment of herpesviruses and other dsDNA viruses that are associated with malignancies: EBV HPV CMV
- **Active Discovery Programs**
  - Lipid Conjugate Technology enables oral dosing and reduced toxicity
  - Chemical Library of >10,000 unique compounds
- **As of 9/30/15, $378 million available to fund operations**

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Today's Agenda

- Review data from SUPPRESS presented at BMT
- Review additional data from ongoing analyses to better understand the failures and successes with some subgroups of the SUPPRESS patients
- Discuss how some of these learnings can help us move forward in CMV prevention in HCT recipients and other populations

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Brincidofovir: CMX001, BCV

- Viral DNA polymerase inhibitor that achieves high intracellular antiviral concentrations, active against dsDNA viruses in vitro
- Orally bioavailable, no evidence of myelotoxicity or nephrotoxicity
- Not a substrate of organic anion transporter 1 (OAT-1)
- Phase 2 dose escalation trial demonstrated that BCV 100 mg twice weekly beginning after engraftment through day +90 significantly prevented CMV events vs. placebo
  - 10% vs. 37% (p=0.001); completion rate, 60% vs. 54%
  - Diarrhea was dose limiting toxicity at 200 mg twice weekly
  - Safety Monitoring and Management Plan (SMMP) incorporated in BCV 100 mg BIW cohort, with successful resumption of dosing in 90% of subjects

Marty et al, NEJM, January 2013
Beadle et al AAC 2002;46:2381-6.

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Brincidofovir: Potent *In Vitro* Activity Against DNA Viruses

Viral Family	Virus	Brincidofovir	Cidofovir	Ganciclovir*	Foscarnet	Acyclovir	Maribavir	Letermovir
Herpes	Cytomegalovirus	0.001	0.4	3.8	50-800	>200	0.31	0.005
	Epstein-Barr Virus	0.03	65.6	0.9	<500	6.2	0.63	>10
	Human Herpesvirus 6	0.003	2.7	5.8	16	10	Inactive	>10
	Human Herpesvirus 8	0.02	2.6	8.9	177	>100	Inactive	—
	Herpes Simplex Virus 1	0.01	3.0	0.7	92-95	3.8	Inactive	>10
	Herpes Simplex Virus 2	0.02	6.5	2.5	91-96	4.4	Inactive	>10
	Varicella Zoster Virus	0.0004	0.5	1.3	39.8	3.6	Inactive	>10
Adenovirus	Adenovirus (AdV-B7)	0.02	1.3	4.5-33	Inactive	>100	—	>10
Polyoma	BK Virus (BKV)	0.13	115	>200	Inactive	>200	—	—
	JC Virus (JCV)	0.045	>0.1	—	Inactive	—	—	—
Papilloma	Human Papillomavirus	17	716	Inactive	—	Inactive	—	—
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.

Data are compiled from multiple sources and include multiple materials and methodologies.

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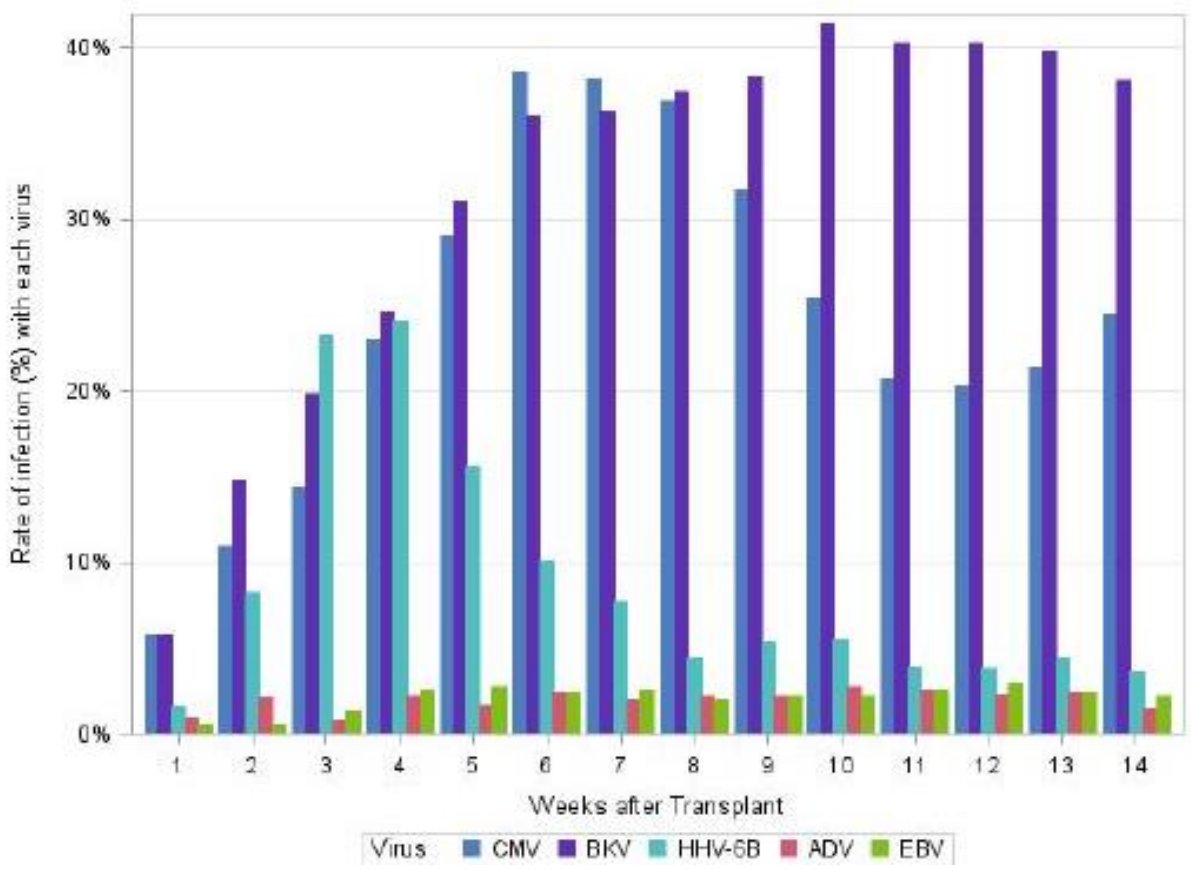
DNA Viral Infections Are Frequent, Persistent and Associated with Mortality after Allo-HCT

- Weekly plasma samples through 100 days post-HCT were tested at the FHCRC for 404 HCT recipients
- Multiple DNA virus detection was associated with an increased mortality risk, even after controlling for acute GVHD
- Improved prevention strategies are needed



Hill J et al. Tandem BMT 2016, Honolulu, HI.

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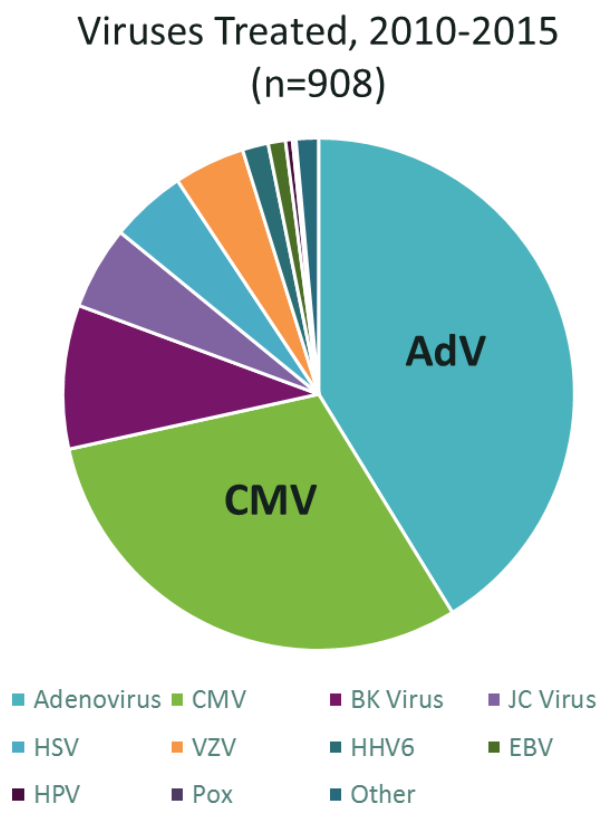
Continued Unmet Medical Need for Brincidofovir Demonstrated Through Expanded Access and EINDs



- Over 900 patients have received brincidofovir for life-threatening DNA viral infections through Expanded Access Trials or Emergency INDs (EIND)
- ***Currently receiving 50-80+ requests/month***
- No alternative treatment available for these infections
- Provides safety database for use of brinci in a broad patient population to support adult and pediatric dosing in the event of a smallpox outbreak

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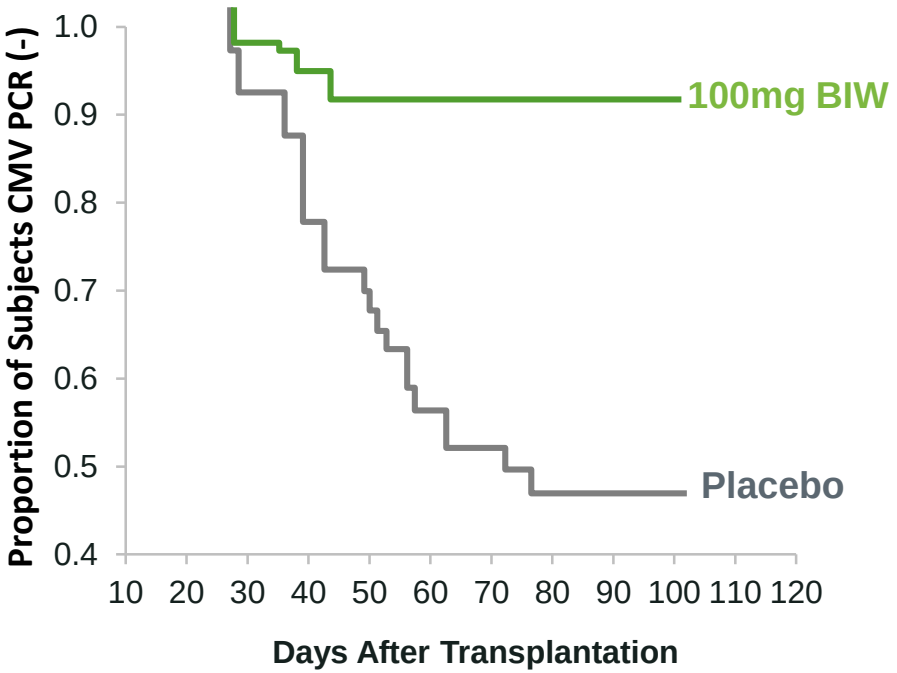
Successful CMV Prevention in Dose-Ranging Phase 2 Study

- High risk allogeneic HCT recipients (CMV R+)
- BCV 100 mg BIW selected on basis of CMV suppression, safety, and tolerability
- No nephrotoxicity – improved GFR compared to pbo
- Hematologic safety – which allowed earlier dosing in SUPPRESS to prevent viral reactivation in first weeks after transplant
- No resistance detected

Brincidofovir Prevented CMV Reactivation in HCT Recipients in Study 201



Marty et al, NEJM, January 2013
Beadle et al AAC 2002;46:2381-6.

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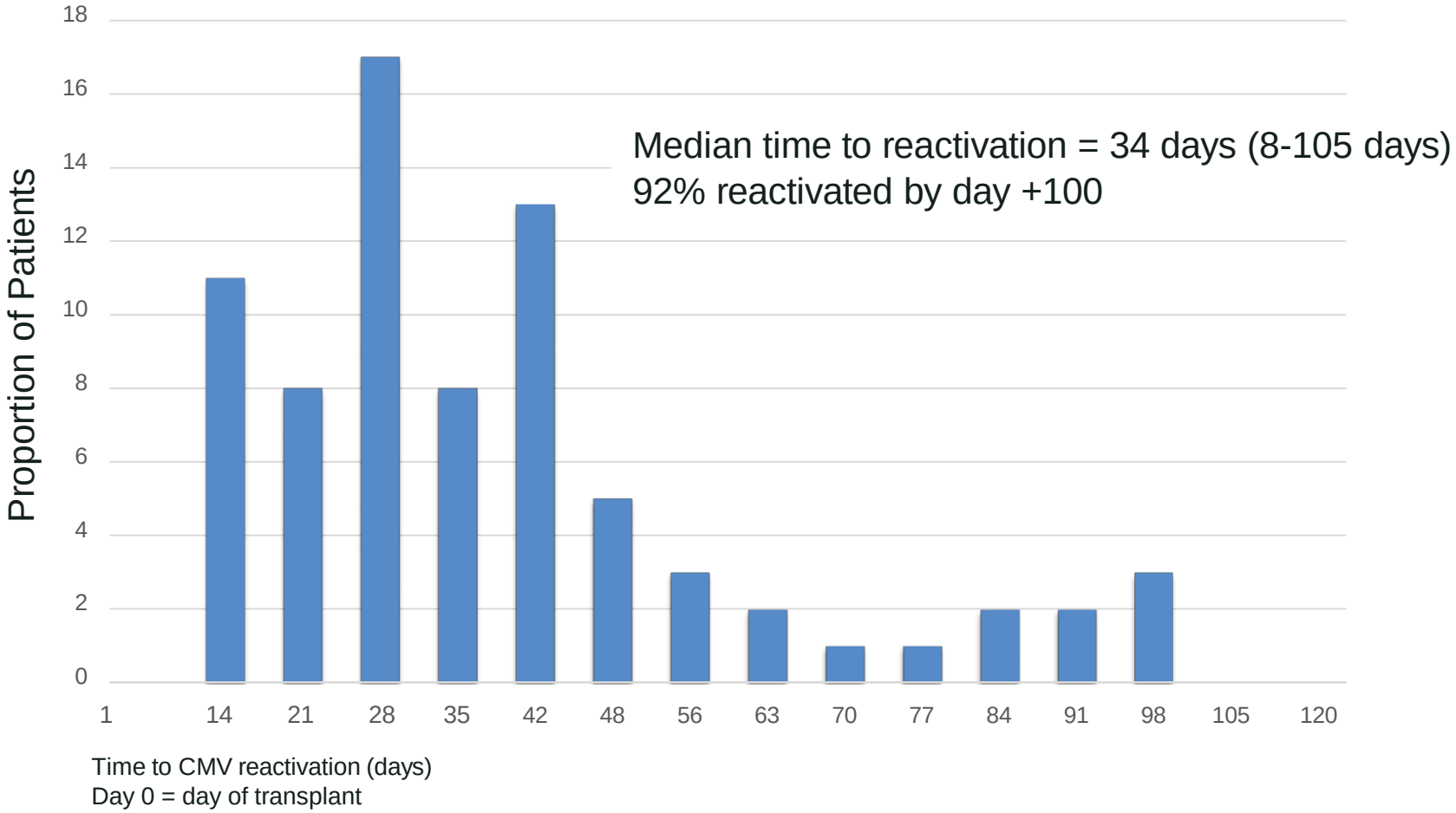
Earlier Dosing After Transplant Based on High Rate of Early CMV Reactivation



Jain et al; NIH BMT Tandem March, 2014

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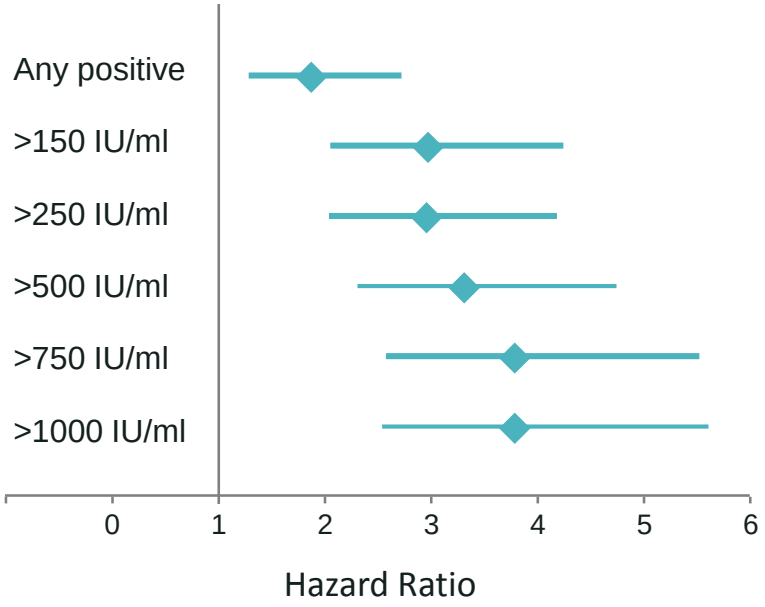
CMV Reactivation Increases Risk of Mortality 2X in HCT Recipients

- Any positive plasma CMV DNA was associated with two-fold hazard for mortality, with higher HR observed in those with higher CMV viral loads
- Non-relapse mortality was 18% at one year (167/926)

Hazard of Non-Relapse Mortality at One Year by CMV Viral Load



FHCRC, 2007-2013
Green ML et al. ICAAC 2014, Washington DC.

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SUPPRESS

BRINCIDOFOVIR FOR PREVENTION OF CYTOMEGALOVIRUS (CMV) AFTER ALLOGENEIC HEMATOPOIETIC CELL TRANSPLANTATION IN CMV-SEROPOSITIVE PATIENTS:

A RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED, PARALLEL GROUP PHASE 3 TRIAL

Francisco M. Marty, Drew J. Winston, Roy F. Chemaly, Michael J. Boeckh, Kathleen M. Mullane, Tsiporah B. Shore, Genovefa A. Papanicolaou, Marion E. Morrison, Thomas M. Brundage, and Herve Mommeja-Marin

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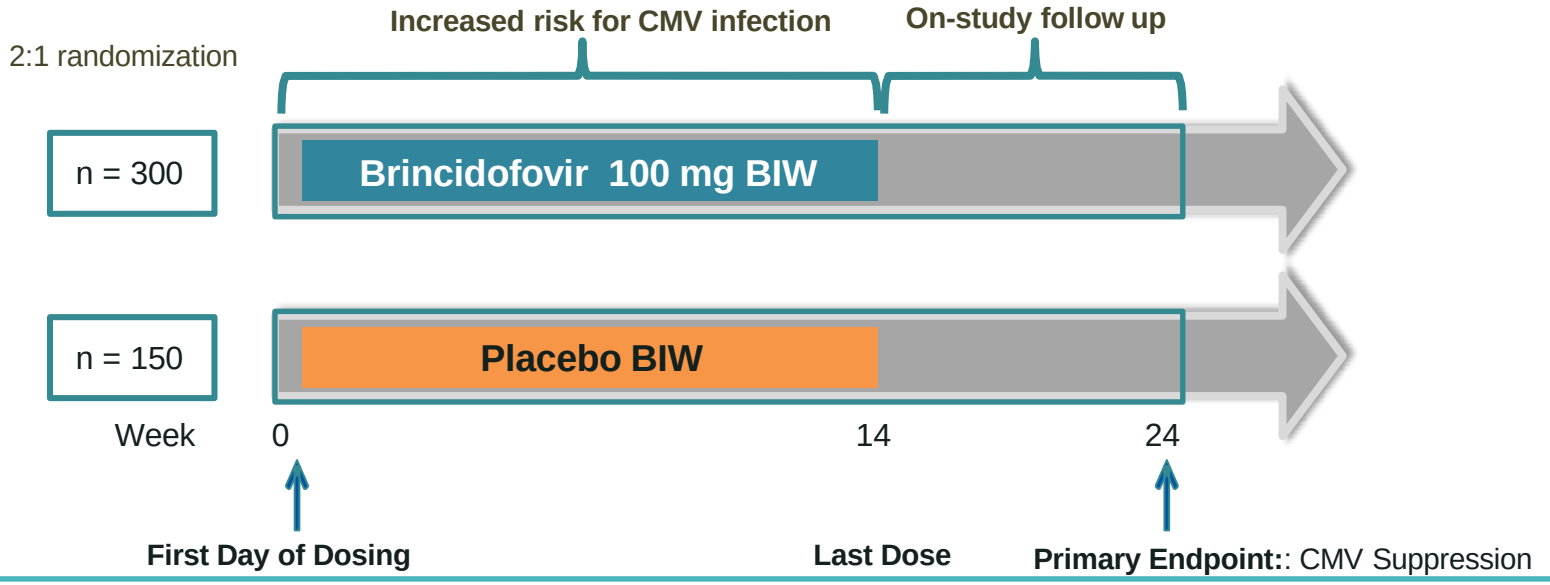
Phase 3 SUPPRESS Trial

- **Population:** High-risk allogeneic HCT recipients, evidence of prior CMV infection (CMV R+)
- **Primary endpoint:** Prevention of CMV infection through Week 24
- **Design:** Superiority vs. current standard of care (placebo and monitoring)
- **Power:** >85% power to detect 50% reduction in CMV events vs. placebo
- **Dosing:** Began when patient can swallow tablet; twice-weekly through Week 14



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SUPPRESS Stratification: Risk for Clinically Significant CMV Reactivation

- **Higher Risk Likelihood**
  - T-cell depletion
  - Cord blood or haploidentical HCT
  - HCT from unrelated or mismatched donors
  - Use of ATG or alemtuzumab
  - ≥1 mg/kg of prednisone or equivalent for treatment of acute GVHD or other conditions
- **Lower Risk Likelihood**
  - HCT from matched related donors without higher likelihood covariates

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SUPPRESS Phase 3 Results

- During the on-treatment period through Week 14 after HCT:
  - Fewer subjects in the brincidofovir arm had CMV reactivation, consistent with the positive antiviral effect of the compound seen in Phase 2
- During the 10 weeks off-treatment from Week 14 to Week 24:
  - An increase in CMV infections was observed in subjects randomized to BCV
- At Week 24, a numerical but non-statistically significant increase in mortality was noted in subjects randomized to BCV
- CMV infections and mortality in the brincidofovir arm appear to be driven by diagnoses of graft-versus-host-disease (GVHD) and a significantly higher use of corticosteroids and other immunosuppressive agents than in the control arm
  - Use of high-dose corticosteroids results in further immune suppression and is known to increase the rate of late CMV infection

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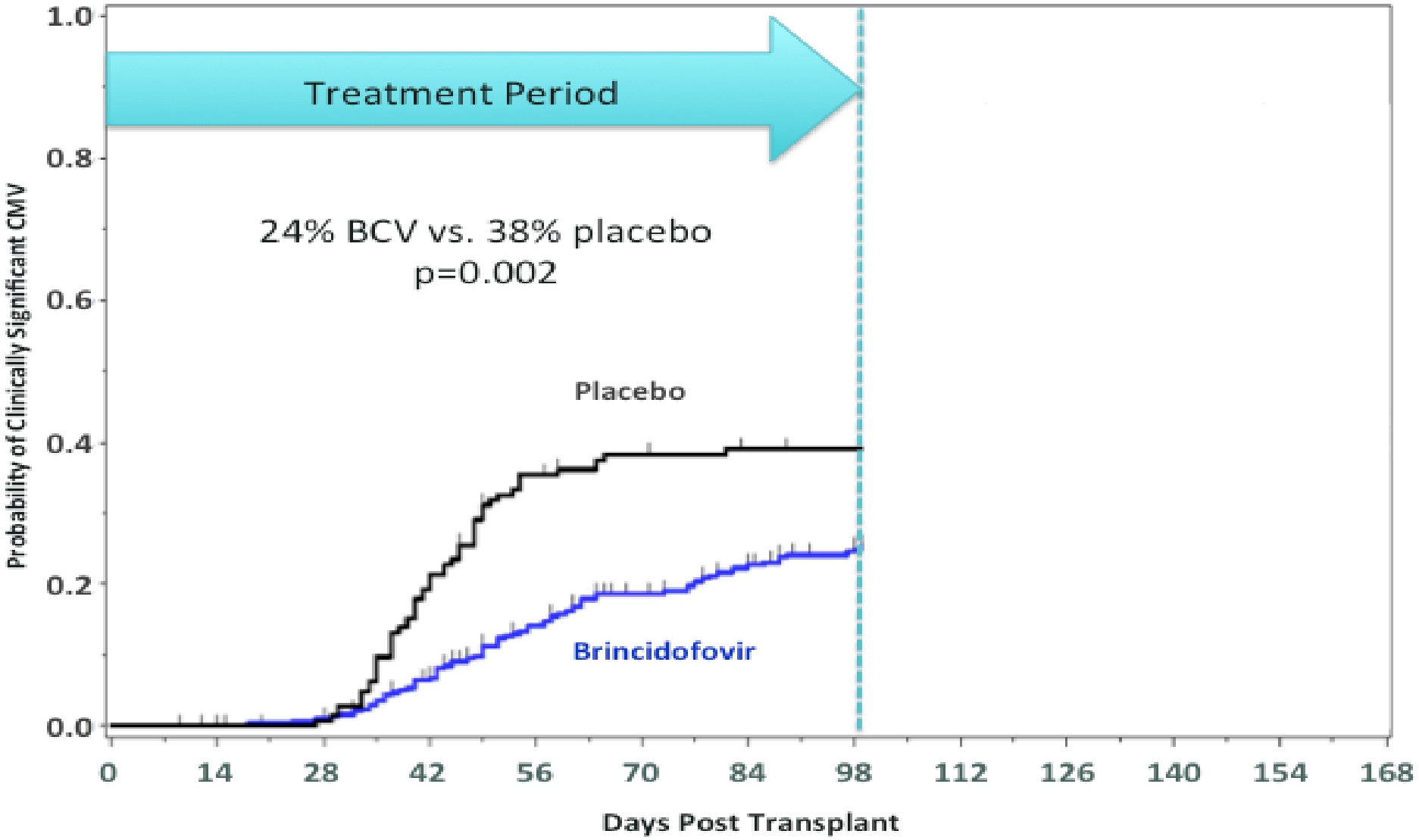
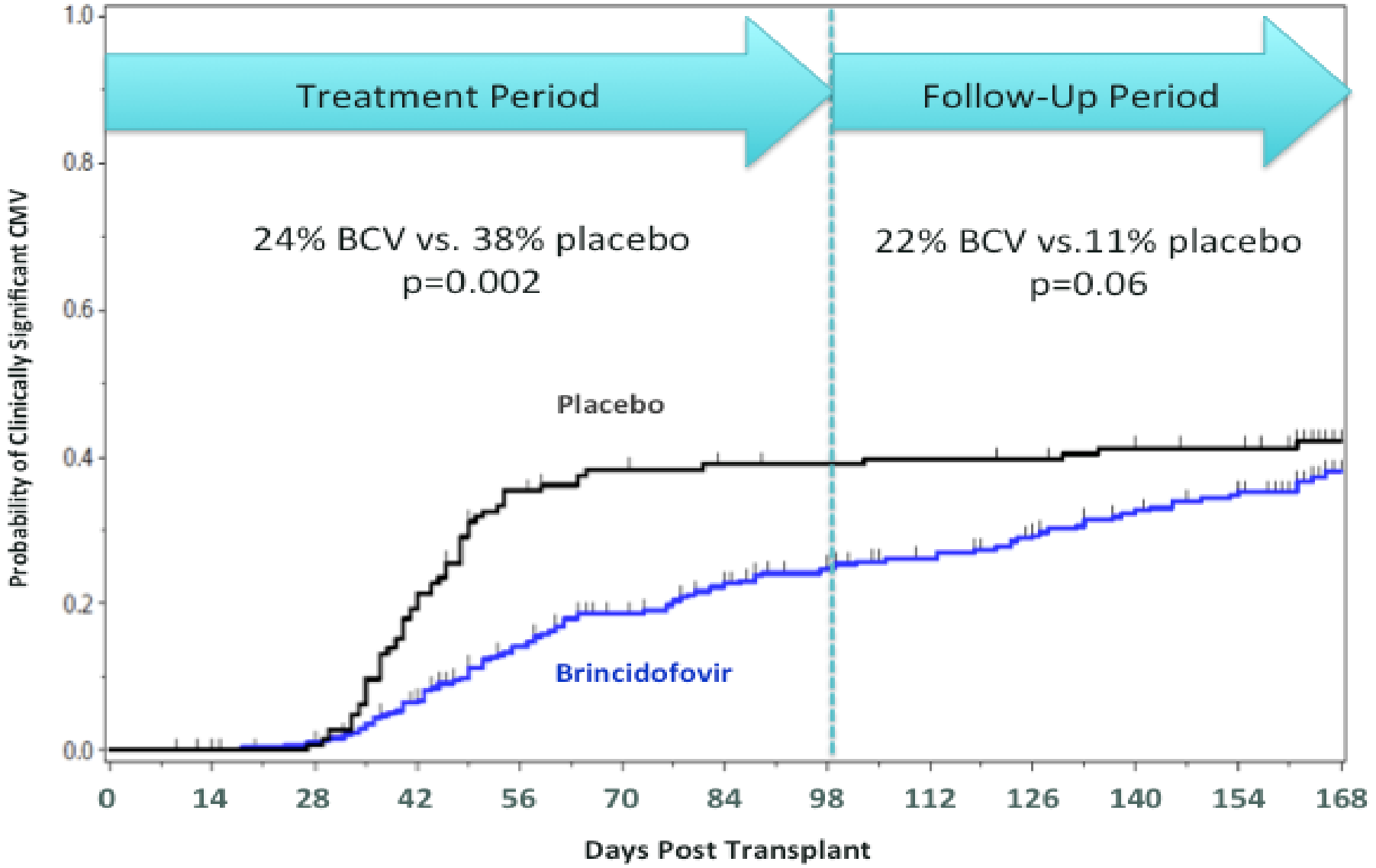
SUPPRESS: Fewer Subjects Reactivated CMV During On-drug Period



SUPPRESS: More Infections Occurred on BCV During Off-drug Period



Graft-vs-Host-Disease (GVHD) in HCT

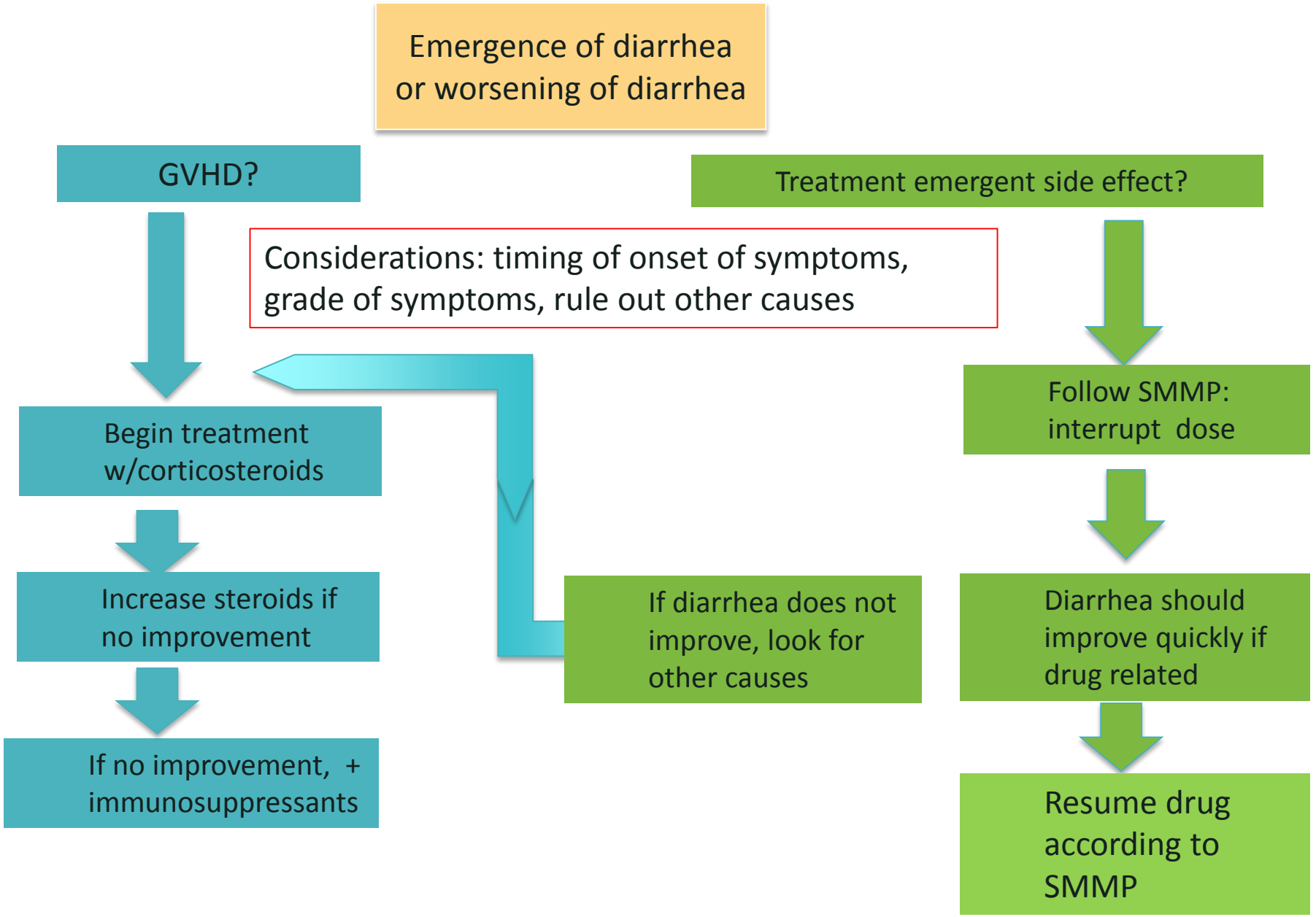
- GVHD occurs when newly transplanted immune cells from the donor attack the recipient's body
- GVHD is a common complication after allogeneic HCT
- 1-year mortality >70% for Gr 3-4 GVHD
- Symptoms of acute GVHD include:
  - Abdominal pain, nausea/vomiting or diarrhea
  - Skin rash
  - Liver injury including jaundice
- There is no definitive test for GVHD, clinical diagnosis +/- biopsy
- Treatment: corticosteroids and other immune suppressive drugs which increase risk of bacterial, fungal, and viral infections
- Strong desire to treat early (grade 1-2) due to high mortality in grade 3-4 GVHD

Graft-vs-Host-Disease (GVHD) in HCT

- Approaches to reduce the risk of GVHD in allogeneic stem cell patients include:
  - *Ex vivo:* T-cell depletion to prevent T-cells from attacking the new host
  - *In vivo:* ATG or alemtuzumab to decrease T-cell activity against the host
- Effective approach but increases risk of CMV infection in patients so antiviral therapy imperative

- GVHD does not occur in:
  - Autologous stem cell transplants (HCT)
  - Transplants of solid organs (such as kidneys)
  - Patients with DNA viral infection who have not had allo HCT

How to Assess Diarrhea in SUPPRESS?



How to Assess Diarrhea in SUPPRESS?

Emergence of diarrhea
or worsening of diarrhea

GVHD?

Treatment emergent side effect?

Considerations: timing of onset of symptoms,

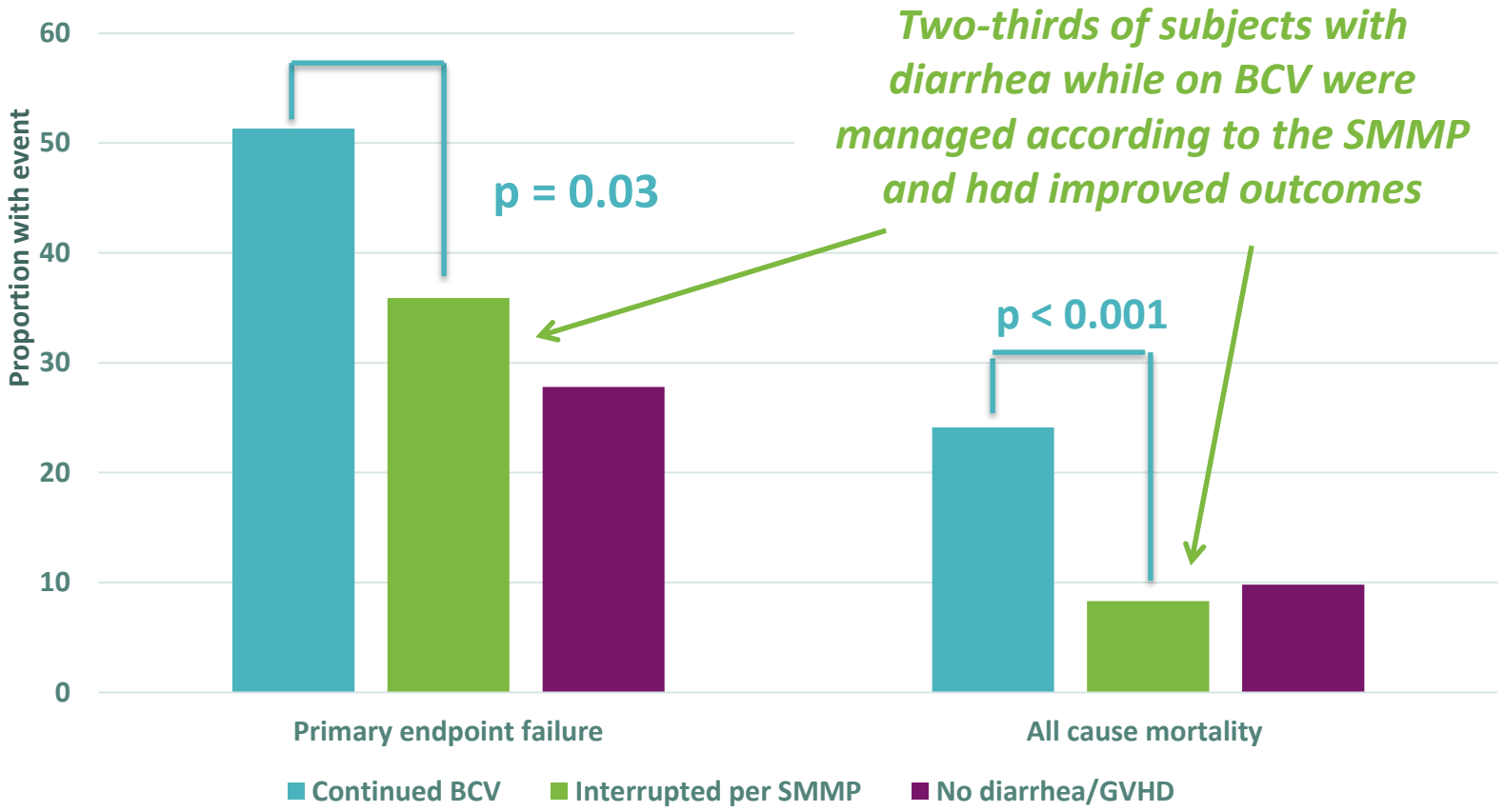
The median cumulative exposure to corticosteroids was 8-fold higher in subjects on the BCV arm than those on placebo

if

immunosuppressants

Resume drug according to SMMP

Among Subjects on BCV With Diarrhea, Interruption of Study Drug Lead to CMV Prevention and Lower Mortality



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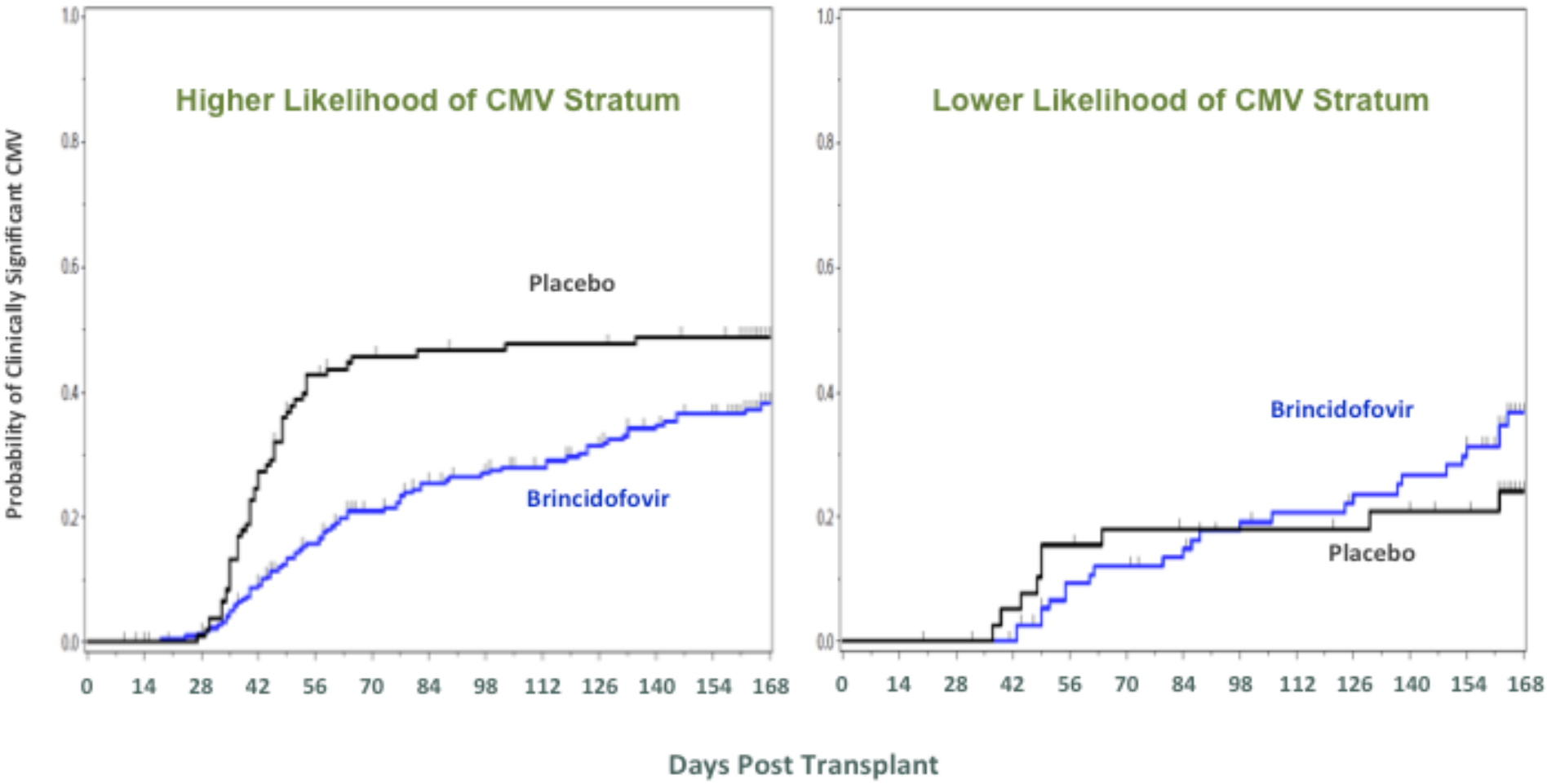
Patients at Higher Risk for Developing CMV Had Better Results on Brincidofovir



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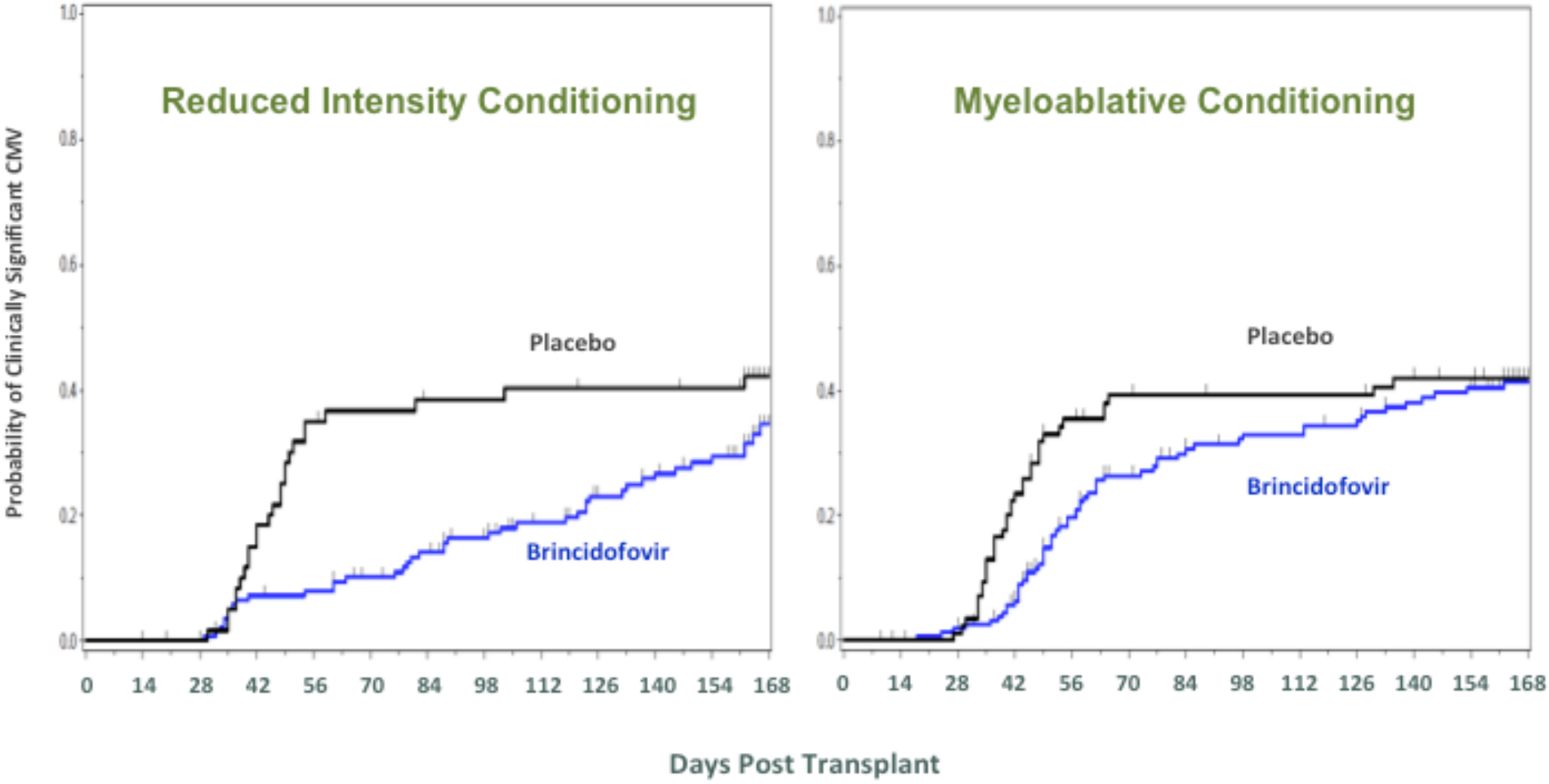
Non-myeloablative HCT Recipients Had Better Results on Brincidofovir

Time to clinically significant CMV infection



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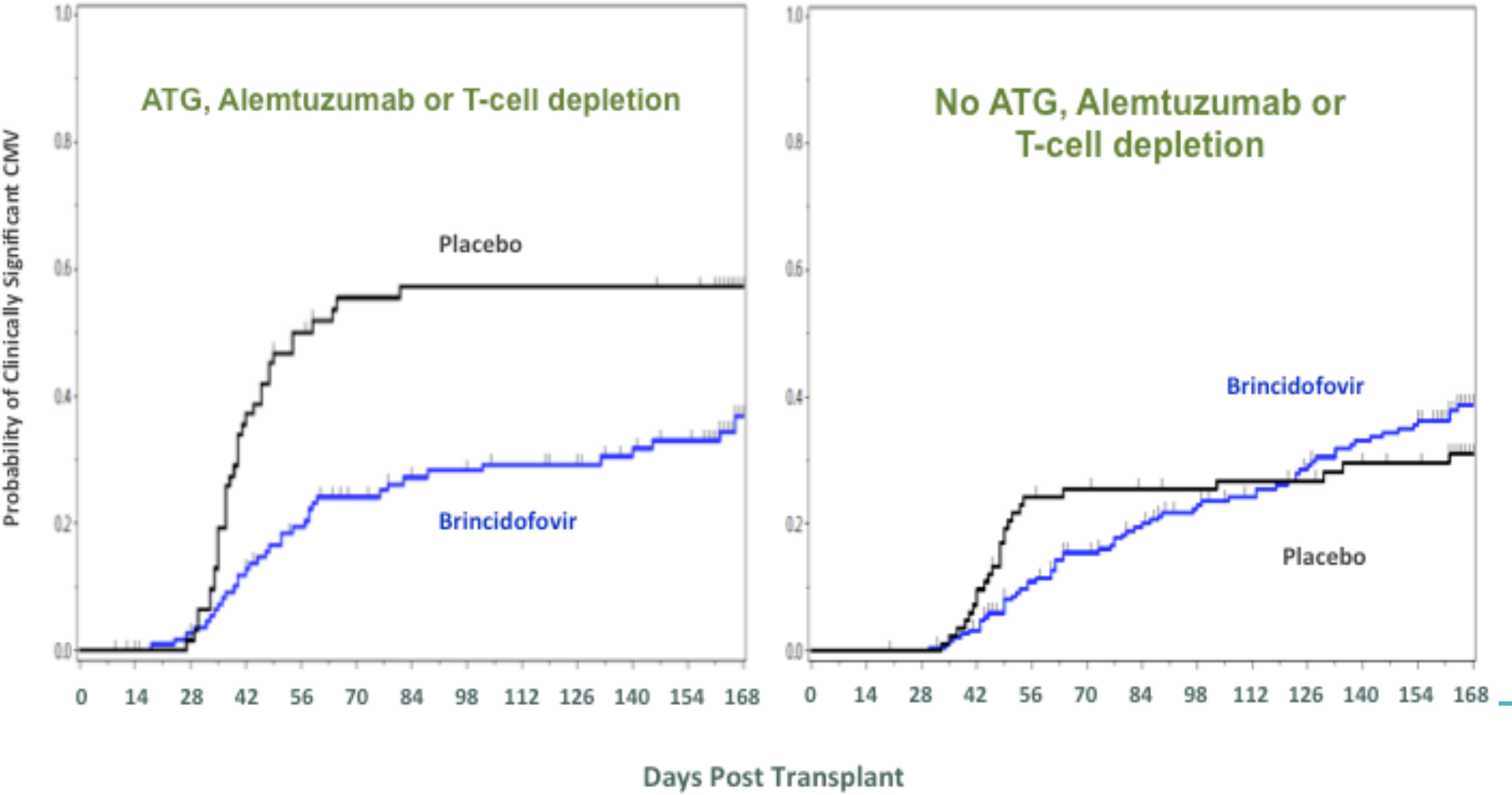
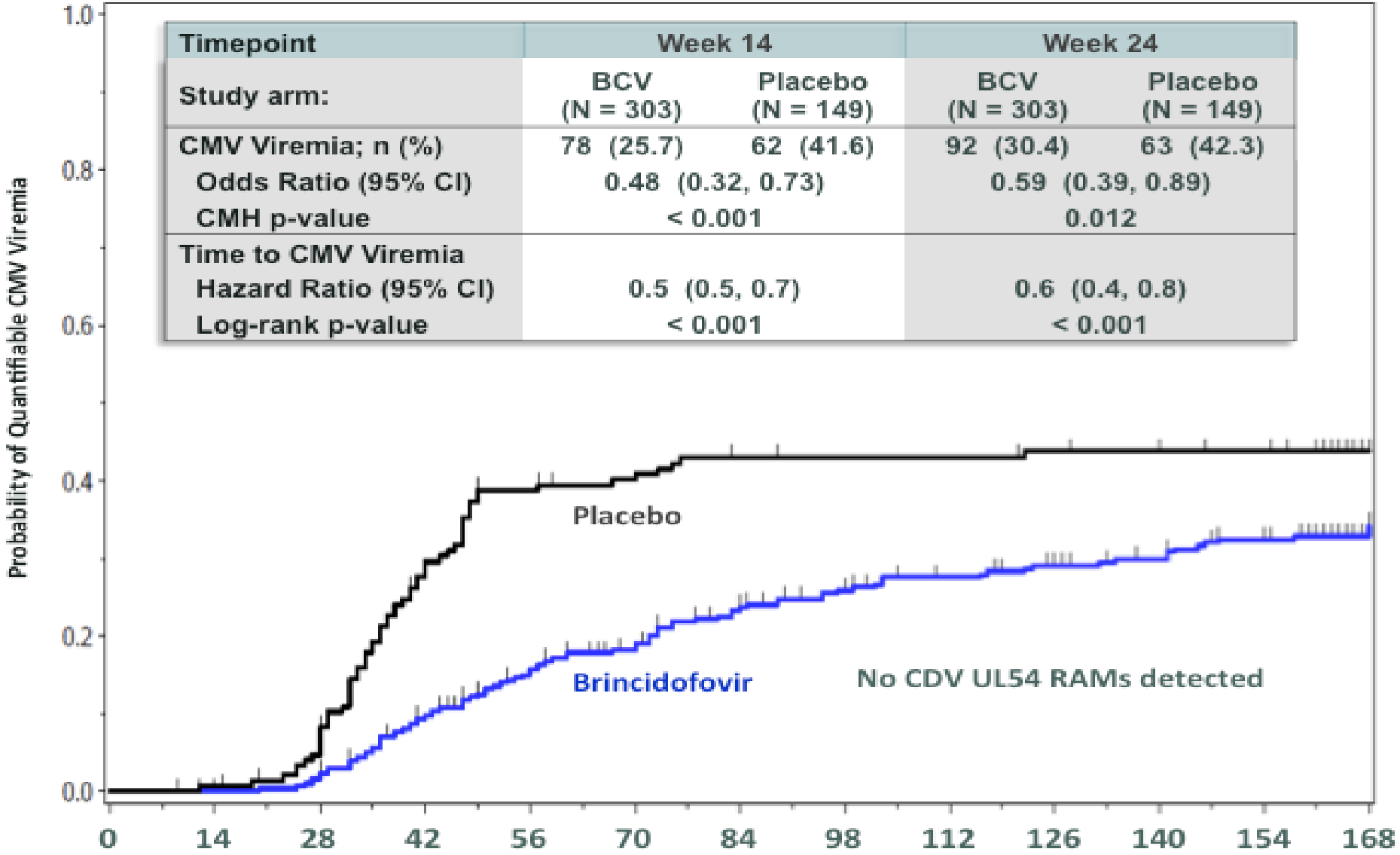
T-cell Depleted Patients (*in vivo* or *ex vivo*) Had Better Results on Brincidofovir

Time to clinically significant CMV infection



Brincidofovir Significantly Reduced CMV Viremia (≥151 c/mL) Through 24 Weeks Post-Transplant

Timepoint	Week 14		Week 24	
Study arm:	BCV (N = 303)	Placebo (N = 149)	BCV (N = 303)	Placebo (N = 149)
CMV Viremia; n (%)	78 (25.7)	62 (41.6)	92 (30.4)	63 (42.3)
Odds Ratio (95% CI)	0.48 (0.32, 0.73)		0.59 (0.39, 0.89)	
CMH p-value	< 0.001		0.012	
Time to CMV Viremia				
Hazard Ratio (95% CI)	0.5 (0.5, 0.7)		0.6 (0.4, 0.8)	
Log-rank p-value	< 0.001		< 0.001	



Drug-related Diarrhea or Acute GVHD?

- **Did diarrhea lead to empirical GVHD treatment?**
  - Patients were often treated for acute GVHD, with or without holding BCV
  - Following the SMMP and temporarily interrupting BCV improved outcomes
- **Was GI GVHD misdiagnosed?**
  - Gut biopsy showed apoptosis attributed to acute GVHD, but may in fact have been BCV-related apoptosis (e.g., mycophenolate)
- **Did BCV induce GVHD?**
  - BCV could theoretically induce host mucosal injury that generates an alloimmune response, although there was no increase in skin GVHD
  - ***However, steroids plus continued BCV did not lead to resolution of diarrhea, suggesting this was not gut GVHD***

GVHD Events on BCV were Predominantly Gut, not Skin, Suggesting Diagnosis was Driven by Diarrhea

N (%)	Brincidofovir (n=303)			Placebo (n=149)		
GVHD Stage	Skin	Liver	Gut	Skin	Liver	Gut
Stage 1	49 (16.2)	3 (1.0)	88 (29.0)	24 (16.1)	1 (0.7)	28 (18.8)
Stage 2	42 (13.9)	14 (4.6)	40 (13.2)	18 (12.1)	0	7 (4.7)
Stage 3	22 (7.3)	7 (2.3)	33 (10.9)	8 (5.4)	3 (2.0)	2 (1.3)
Stage 4	0	6 (2.0)	13 (4.3)	0	3 (2.0)	3 (2.0)

Safety: Overall Summary of Adverse Events

	Brincidofovir	Placebo
N (%)	303	149
TEAE, any grade	302 (99.7)	146 (98.0)
CTCAE grade ≥3	203 (67.0)	56 (37.6)
Serious TEAE	173 (57.1)	56 (37.6)
TEAE leading to drug discontinuation	79 (26.1)	11 (7.4)
TEAE leading to drug interruption or change	136 (44.9)	22 (14.8)

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Conclusions: Safety

- Brincidofovir had no evidence of myelotoxicity or nephrotoxicity
- Lower GI adverse events occurring on the BCV arm had an increased frequency of diagnosis and treatment for acute GVHD
  - Earlier BCV administration to prevent early CMV events led to a increased rate of GI events, most notably in patients who received myeloablative conditioning
  - Treatment for GVHD with high-dose corticosteroids and other immune suppressive agents was associated with increased morbidity, mortality and post-prophylaxis CMV events
  - **Closely following the protocol's SMMP decreased the proportion of patients who met the primary endpoint and rate of all-cause mortality**

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SUPPRESS: Divergence from Ph 2 was Driven by Presumptive Diagnosis of GVHD, Treatment with Steroids

- GI adverse events known to occur with brincidofovir may mimic the presentation of gut GVHD:
  - A GI biopsy from a single kidney transplant recipient randomized to BCV was interpreted by the local pathologist as consistent with viral colitis or GVHD
  - Responded to interruption of study drug

- Increased rate of presumptive gut GVHD in BCV cohort, but
  - Many patients were diagnosed based on clinical presentation
  - Low incidence of skin rash, a much more common sign of GVHD
- Diarrhea persisted in those patients who continued BCV dosing
  - Lead to increased steroid use and some second-line immune suppressing agents (monoclonal Ab, biologics, etc.)

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What have we learned?

- **Two-thirds of patients enrolled in SUPPRESS were T-cell depleted, had reduced intensity conditioning, or had ATG or Campath.**
  - *These patients had better outcomes with brincidofovir.*
- **Three-quarters of patients in the brincidofovir arm were classified as being at greater risk for developing CMV**
  - *These patients had better outcomes with brincidofovir.*
- **Management of patients according to the SMMP was associated with better outcomes**

Enhanced education on adherence to the SMMP will be critical moving forward

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Next Steps in Allogeneic HCT

- **Continue analyses to inform future trial designs for prevention and/or treatment of CMV infections**
- **Trials in prevention could include sub-populations where benefit was observed**
  - These populations account for at least **75%** of the patients enrolled in SUPPRESS, and are reflective of the general allogeneic transplant population
- **Trials evaluating treatment of refractory CMV or patients intolerant of current antivirals**
- **Trials using IV brincidofovir initially in prevention to potentially avoid GI issues**
  - ***IV brincidofovir (with oral step-down) may offer advantages by decreasing GI events in the critical first weeks after HCT***

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Brincidofovir Intravenous Formulation

- Bypassing the gut could avoid local irritation and decrease incidence of diarrhea
- Preliminary data from 28 day preclinical study shows that IV BCV has a lower risk of GI effects
  - Maintained body weight during dosing
  - No evidence of injury in preliminary review of the GI tract
- Maintain established brincidofovir benefits of no myelotoxicity, no nephrotoxicity
- FTIH study anticipated 2H2016, bridge to drug levels in plasma from ongoing programs & incorporate into next CMV prevention in HCT

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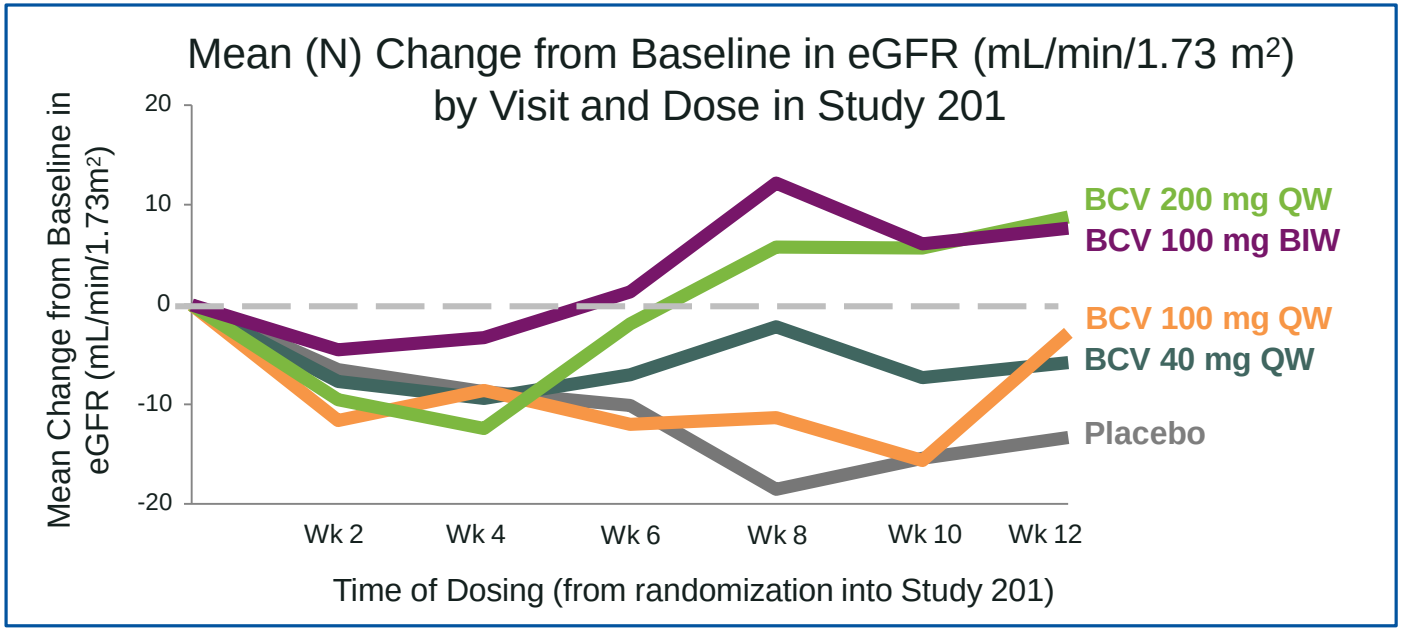
Brincidofovir Improved Renal Function in HCT Recipients: First Clinical Evidence of Potential BCV Effect on BKV



eGFR: estimated glomerular filtration rate

Baseline GFR	Week 2	Week 4	Week 6	Week 8	Week 10	Post-Week 1
Placebo	-7 (56)	-9 (46)	-10 (35)	-19 (36)	-15 (21)	-13 (57)
Brincidofovir 100 mg BIW	-5 (49)	-3 (44)	1 (33)	12 (31)	6 (21)	8 (49)
				p=0.0013	**p=0.0103**	**p=0.0025**

Data from Study 201 presented at BMT Tandem, February 2013

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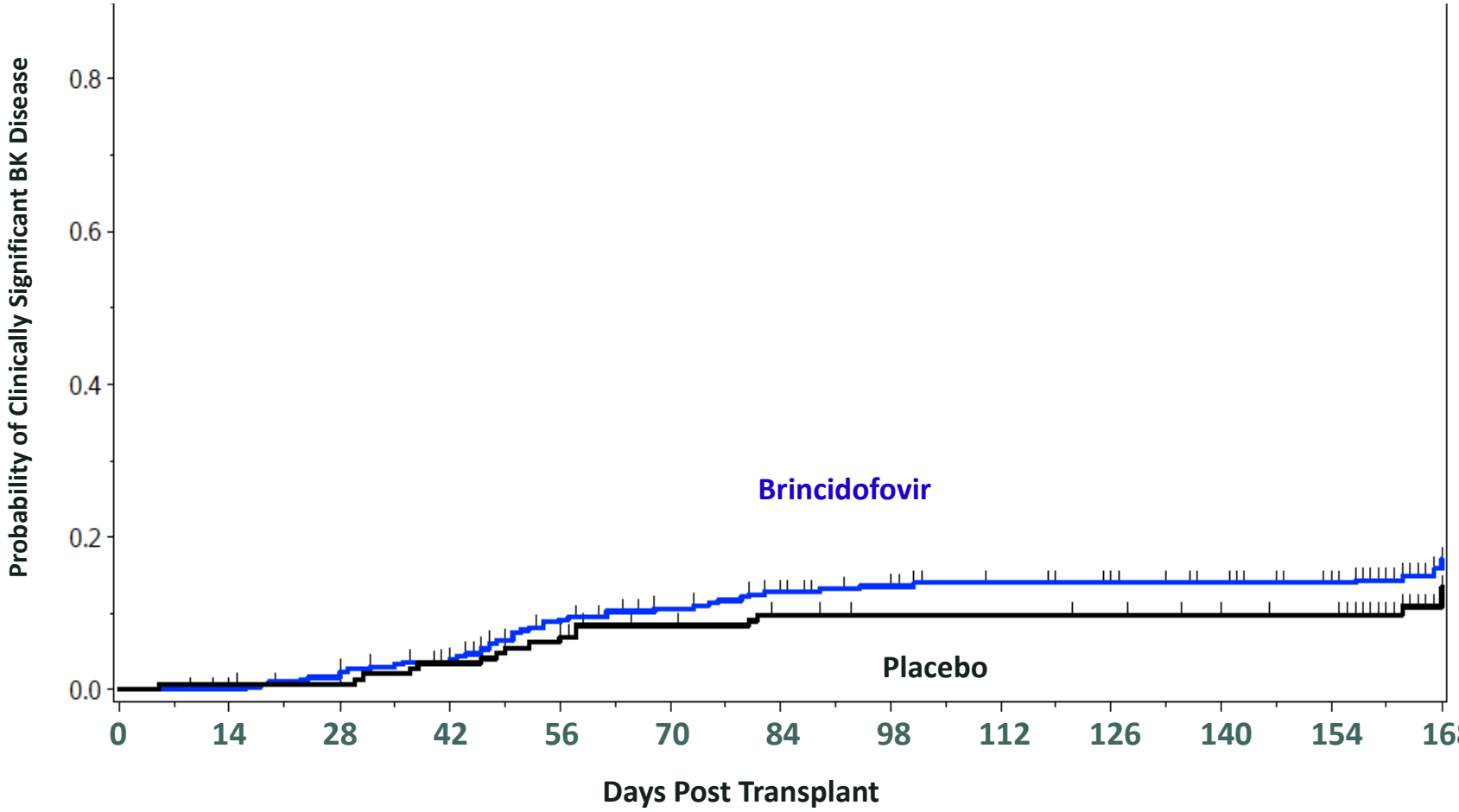
Investigator-reported BK Clinical Events in HCT Recipients (Hemorrhagic Cystitis) were not Significantly Improved on BCV, but…



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Late-breaking Data:
BCV Treated Patients had Lower Incidence of BK Viremia

- Analyzed subjects BKV plasma negative at baseline
  - (N=273 BCV / 132 PBO)
- Limited analysis through Day 56 post-HCT
- Similar length of follow-up between groups
- Incidence of BK viremia: BCV 13% vs PBO 20%
  - Fisher p=0.08, Log-rank 0.06

Next: subgroup analysis by risk factors (including baseline BKV in urine), kidney function over time, explore PK/PD relationships

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Rationale for Stopping the *Current* SURPASS and SUSTAIN Kidney Trials

- BK virus activity and potential for improved renal function demonstrated in Phase 2 HCT trial not as clear in SUPPRESS data to-date
- Desire to understand potential refinements to study design or conduct to increase likelihood of success in SOT trials
- In kidney transplant, anti-rejection drugs can cause diarrhea
  - Although no risk of GVHD in this population, do not want to have confusion with brincidofovir side-effects
- May conduct smaller Phase 2 trial to de-risk outcomes

Next steps: subgroup analysis of SUPPRESS data by risk factors (including baseline BKV in urine), kidney function over time, explore PK/PD relationships

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What Is Ahead For Brincidofovir in 2016?

- Data review with FDA/EMA to define regulatory paths for CMV prevention and/or treatment in HCT and SOT recipients
- IV brincidofovir may provide additional path forward in patients at higher risk of GVHD in the first few weeks after HCT

On upcoming Earnings and Update call we will discuss updates on:

- AdVise & historic control data review with FDA/EMA to define regulatory path for AdV
- Complete smallpox efficacy studies, review potential filing strategy with FDA

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