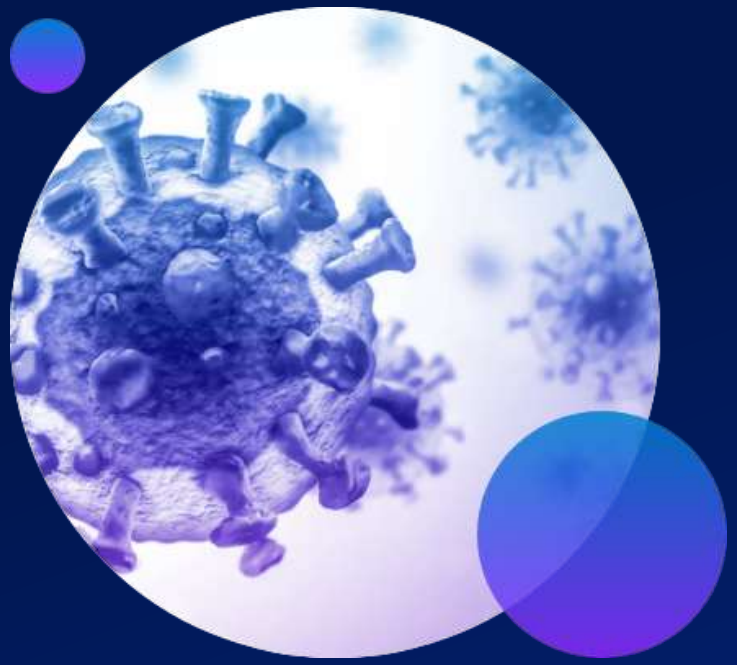
Discovery and Development of Pritelivir, a Novel Treatment Option for Refractory Herpes Simplex Virus Infections

Alexander Birkmann

AiCuris Anti-infective Cures AG

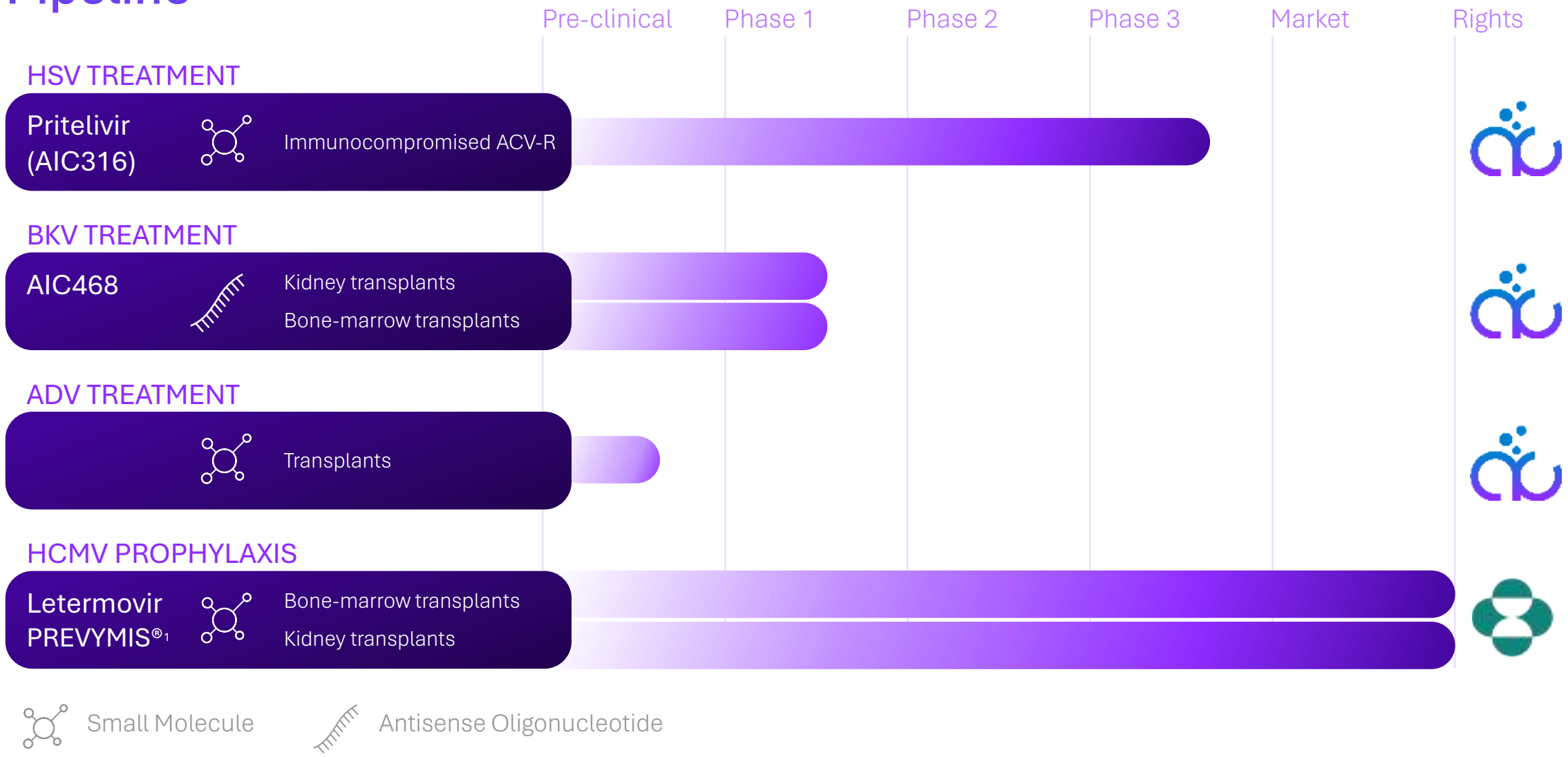
PEG 29/04/2025

AICURIS AT A GLANCE

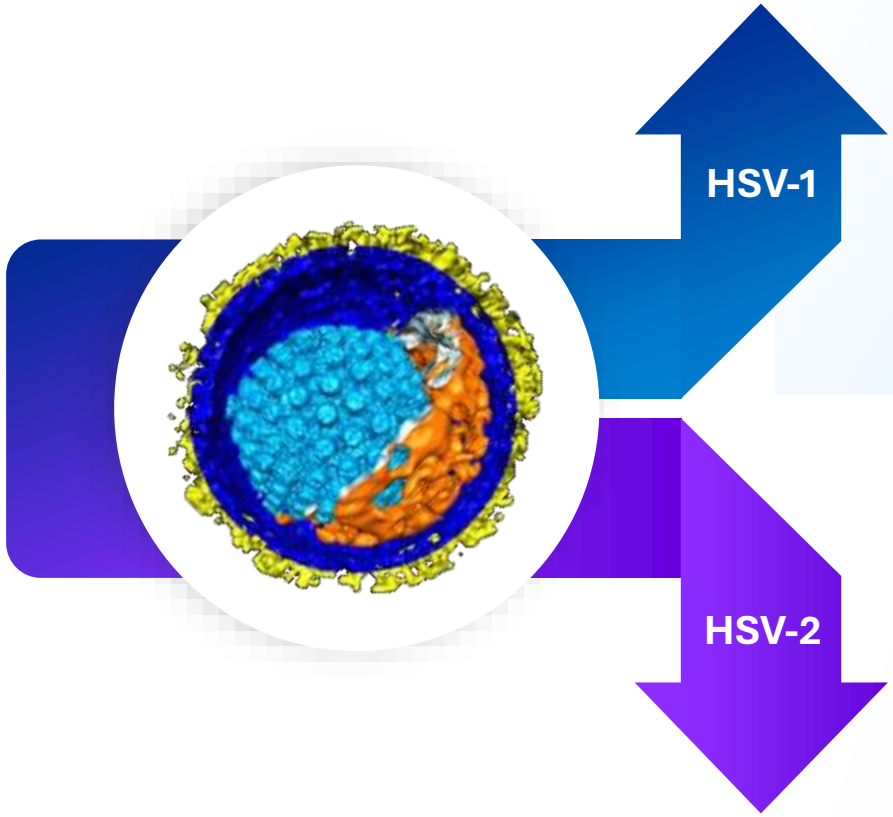


- Privately owned since 2006, clinical-stage biopharmaceutical company with successful development of PREVYMIS®, first-in-class CMV prophylaxis
- Company focused on providing novel anti-viral therapies for a growing number of immunocompromised patients with high unmet medical needs
- Pivotal phase 3 candidate pritelivir with Breakthrough Therapy Designation designed to treat drug resistant & refractory HSV infections
- AIC468, first-in-class anti-sense oligonucleotide, for the treatment of BKV infection in immunocompromised patients in Phase 1
- Executive management and seasoned R&D team with a track record of bringing antivirals to market
- Germany-based with recently formed US subsidiary to prepare for expected US commercial launch of pritelivir

Pipeline


Pre-clinical
Phase 1
Phase 2
Phase 3
Market
Rights
HSV TREATMENT
Pritelivir (AIC316)
Immunocompromised ACV-R
BKV TREATMENT
AIC468
Kidney transplants
Bone-marrow transplants
ADV TREATMENT
Transplants
HCMV PROPHYLAXIS
Letermovir PREVYMIS®1
Bone-marrow transplants
Kidney transplants
Small Molecule
Antisense Oligonucleotide

Herpes simplex virus infections are caused by two widespread viruses causing lifelong latent infections



LABIAL HERPES (COLD SORES)
Global prevalence of HSV-1: 64.2%, **up to 90%** in certain regions and populations.[1]

GENITAL HERPES, TRANSMITTED SEXUALLY
Over 500 million HSV-2 positive people worldwide (global prevalence: 13.3%)[1]

Increasing rates of genital herpes caused by HSV-1.

Standard of care
Currently treated with nucleoside analogs such as acyclovir

Suboptimal therapy
Outbreaks and lesions despite therapy with nucleosides

Resistance
Development of resistance in immunocompromised patients

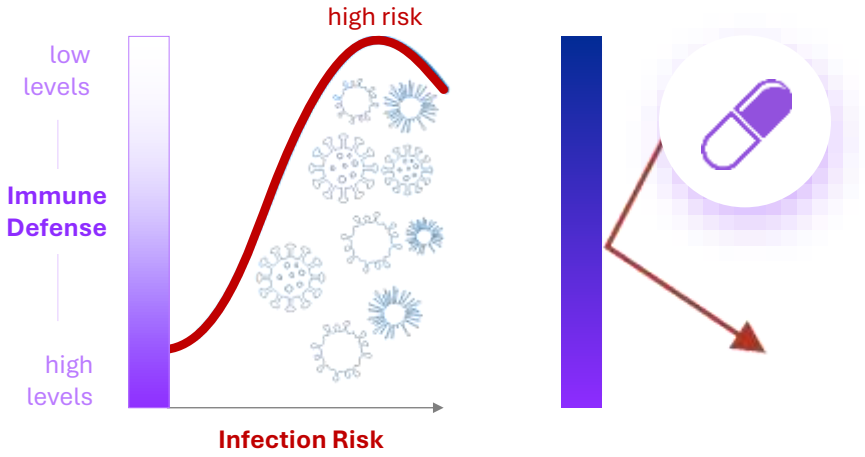
[1]Harfouche *et al.*, 2024

Resistant & refractory HSV infection

High unmet medical need for treatment options in immunocompromised patients

- Low prevalence of resistant HSV in immunocompetent patients (~0.5%)
- **Up to 27%**[1] of IC patients develop drug resistance
  - Due to mutations in TK (95%) or HSV DNA polymerase (5%)
- **More frequent, prolonged & severe lesions**
  - Increased hospitalization rates
  - Risk of dissemination
- **Foscarnet IV (SOC):** high risk of side effects (renal impairment, electrolyte changes, seizures), requires hospitalization with close monitoring
- Patients with **foscarnet resistance or intolerance** currently lack any (approved) therapeutic option

Weakened Immune Defense → **Prolonged HSV outbreaks** → **Drug resistance and/or intolerance** →

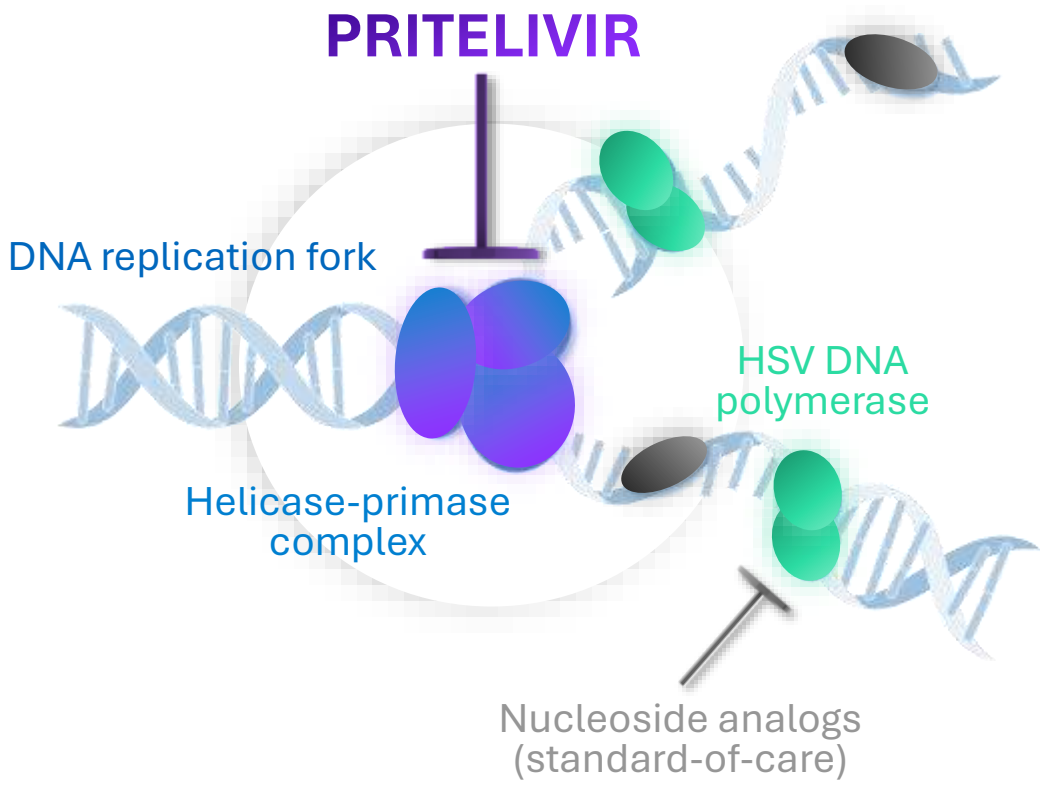


Severely impaired quality of life

[1]Morfin et al., Clinical Virology, 2004

Pritelivir is a small molecule with a novel mechanisms of action

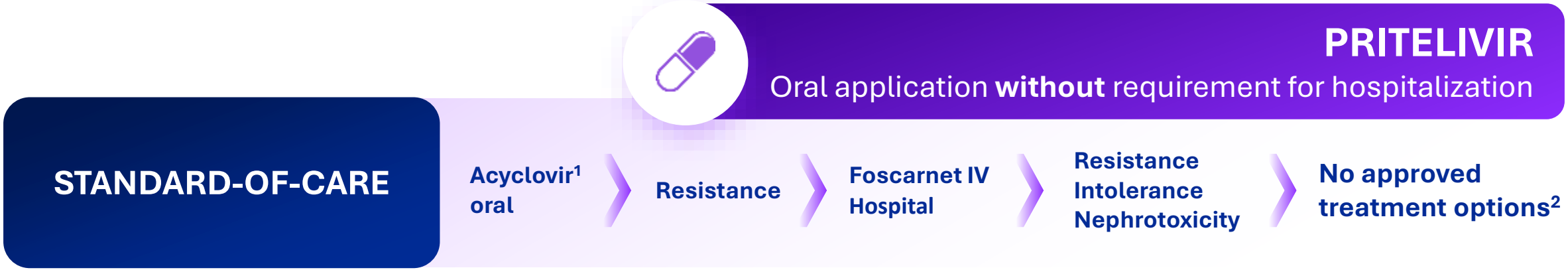
Pritelivir inhibits the viral helicase-primase complex



- Pritelivir is a small molecule inhibiting **viral replication of HSV-1 and HSV-2**
- In contrast to existing drugs, pritelivir targets the **viral helicase-primase complex**
- Pritelivir **prevents infection of uninfected cells** as it does not require activation by viral enzymes
- Pritelivir is **orally bioavailable** with a **long half-life** allowing once-daily dosing

Pritelivir is designed to treat patients with drug-resistant & refractory HSV infections

Patient Journey



NOVEL TREATMENT ALTERNATIVE FOR DRUG-RESISTANT HSV INFECTIONS

- Pritelivir has activity against nucleoside analog and/or foscarnet resistant isolates *in vitro* and *in vivo*

DIFFERENTIATES FROM FOSCARNET BY:

- Favorable bioavailability and half-life with **oral, once daily dosing**
- **Higher healing rates** because of **improved** safety and tolerability profile expected

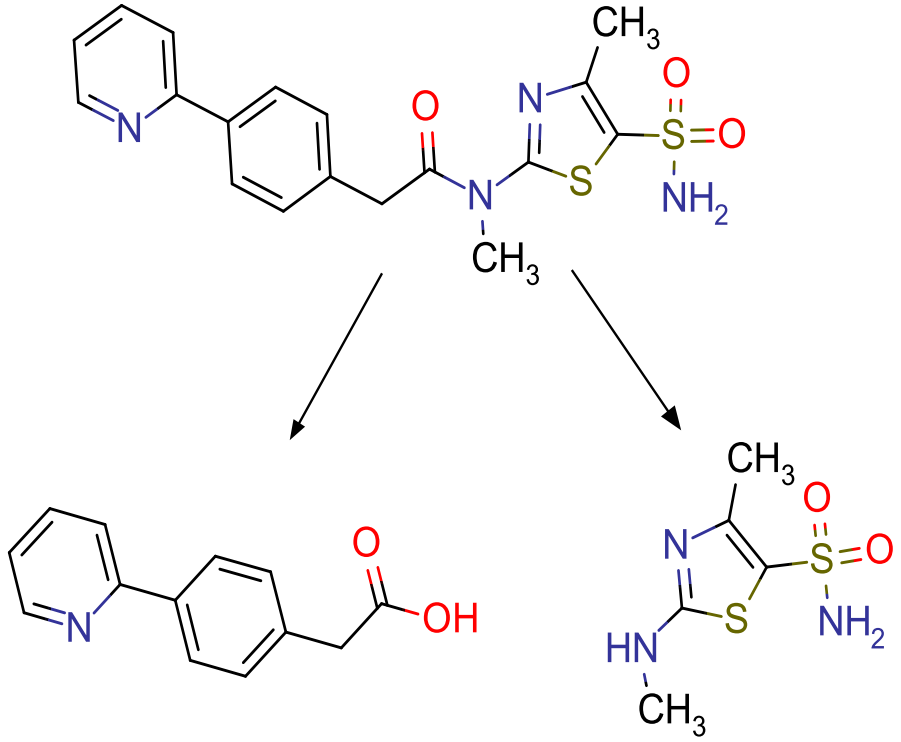
[1]Or prodrugs with increased oral bioavailability (valacyclovir or famciclovir)
[2]Cidofovir or topical Imiquimod as salvage treatments

Pritelivir clinical development

Learnings from pharmacology studies

- Absolute oral bioavailability: 73%
- Terminal elimination half-life: ~60 hours at therapeutic dose level
- Primary metabolism: hydrolysis of the amide bond; glucuronidation and N-demethylation of the inactive hydrolysis products
- Primary route of excretion of the inactive metabolites: renal (renal excretion of pritelivir is negligible)
- PK/PD simulations based on preclinical efficacy data and Phase 1 PK results used for Phase 2 dose selection

PRITELIVIR



Pyridinyl phenyl acetic acid

Amino thiazole sulfonamide

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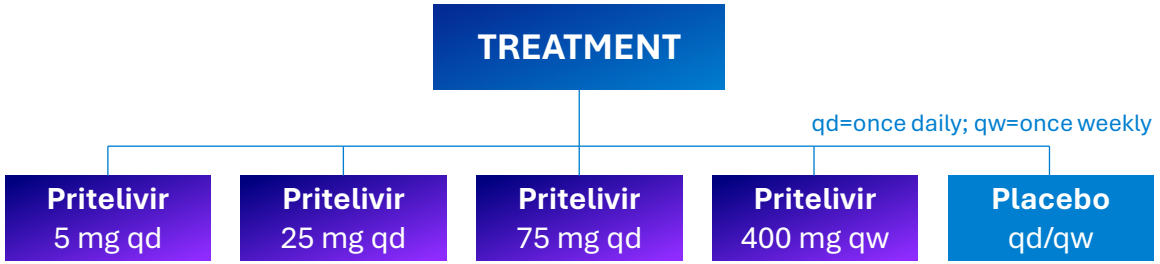
Helicase–Primase Inhibitor Pritelivir for HSV-2 Infection

Anna Wald, M.D., M.P.H., Lawrence Corey, M.D., Burkhard Timmler, M.D., Amalia Magaret, Ph.D., Terri Warren, M.N., Stephen Tyring, M.D., Ph.D., Christine Johnston, M.D., M.P.H., John Kriesel, M.D., Kenneth Fife, M.D., Ph.D., Lawrence Galitz, M.D., Susanne Stoelben, M.D., M.P.H., Meei-Li Huang, Ph.D., Stacy Selke, M.A., Hans-Peter Stobernack, D.V.M., Helga Ruebsamen-Schaeff, Ph.D., and Alexander Birkmann, Ph.D.

Pritelivir Phase 2 proof-of-concept and dose finding trial

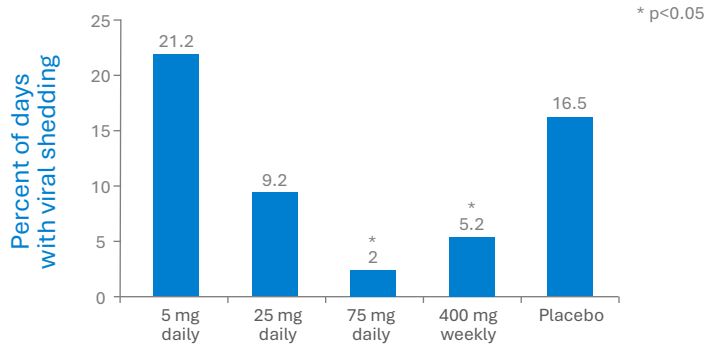
A Double-blind Randomized Placebo-controlled Dose Finding Trial to Investigate Different Doses of Pritelivir in Subjects with Genital HSV Type 2 Infection



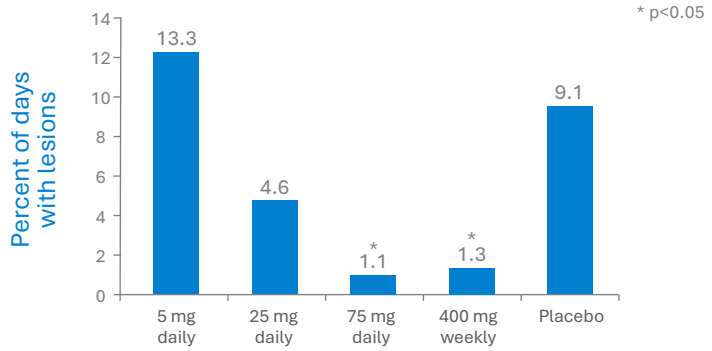
- 156 subjects randomized, 94% completers
- Randomization: 1:1:1:1:1 (pritelivir doses/placebo), parallel groups
- Duration: treatment 28 days; 14 days follow-up until final examination
- Daily genital swabs by trial participants and reporting of any lesion
- **Primary endpoint:** suppression of HSV mucocutaneous shedding

Shedding rate: proportion of days with HSV-positive genital swabs
Lesion rate: proportion of days with lesion reported

SHEDDING RATE (PRIMARY ENDPOINT)



LESIONS RATE (SECONDARY ENDPOINT)



Pritelivir significantly reduced the frequency of HSV shedding and clinical lesions vs. placebo

JAMA | Original Investigation

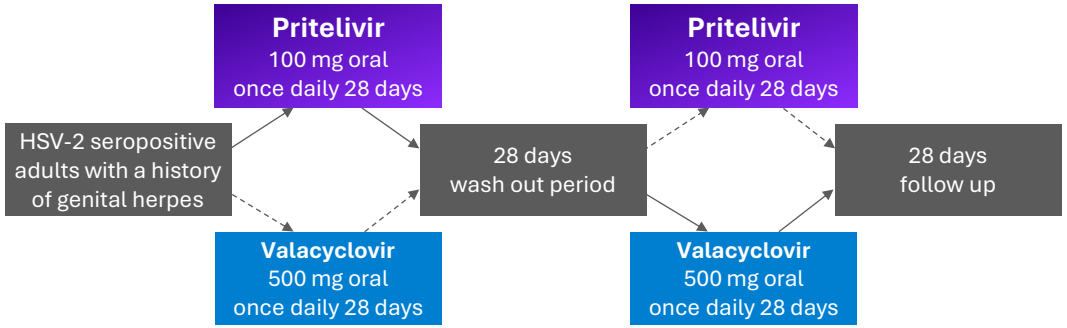
Effect of Pritelivir Compared With Valacyclovir on Genital HSV-2 Shedding in Patients With Frequent Recurrences

A Randomized Clinical Trial

Anna Wald, MD, MPH; Burkhard Timmler, MD; Amalia Magaret, PhD; Terri Warren, ANP; Stephen Tyring, MD, PhD; Christine Johnston, MD, MPH; Kenneth Fife, MD, PhD; Stacy Selke, MA; Meei-Li Huang, PhD; Hans-Peter Stobernack, PhD; Holger Zimmermann, PhD; Lawrence Corey, MD; Alexander Birkmann, PhD; Helga Ruebsamen-Schaeff, PhD

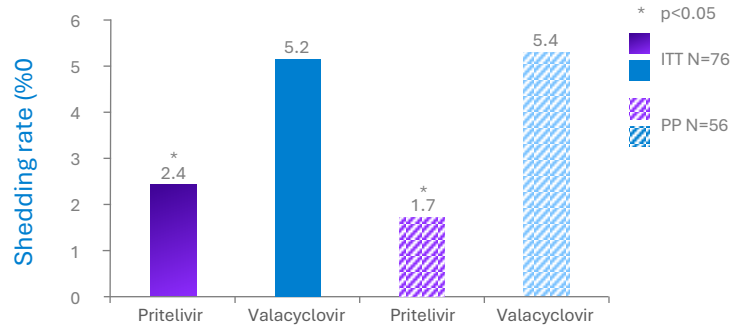
Pritelivir Phase 2B comparative trial versus valacyclovir

A Double-blind, Double Dummy, Randomized Crossover Trial to Compare the Effect of Pritelivir 100 mg Once Daily Versus Valacyclovir 500 mg Once Daily on Genital HSV Shedding in HSV-2 Seropositive Adults

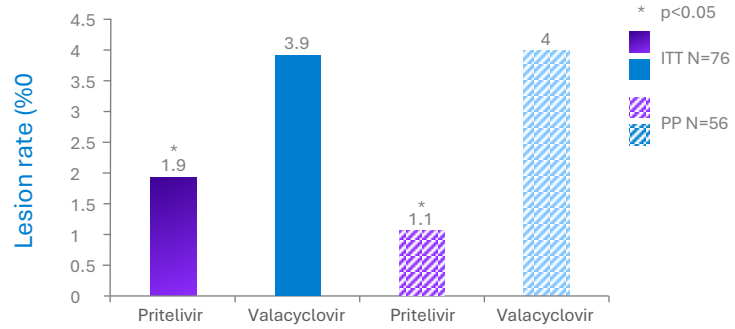


- Pritelivir 100 mg qd vs. valacyclovir 500 mg qd, 91 subjects randomized
- 4-times/day genital swabs by trial participants and reporting of any lesion
- **Primary endpoint:** suppression of HSV mucocutaneous shedding
- Key secondary efficacy endpoints: HSV DNA copy number in positive swabs, proportion of days with lesions
- **Safety outcome:** comparable safety profile (trend to less treatment-emergent adverse events under pritelivir compared to valacyclovir)

SHEDDING RATE



LESIONS RATE



Pritelivir demonstrated superior suppression of HSV and genital lesions vs. valacyclovir

RECRUITING

Trial on Efficacy and Safety of Pritelivir Tablets for Treatment of Acyclovir-resistant Mucocutaneous HSV (Herpes Simplex Virus) Infections in Immunocompromised Subjects (PRIOH-1)

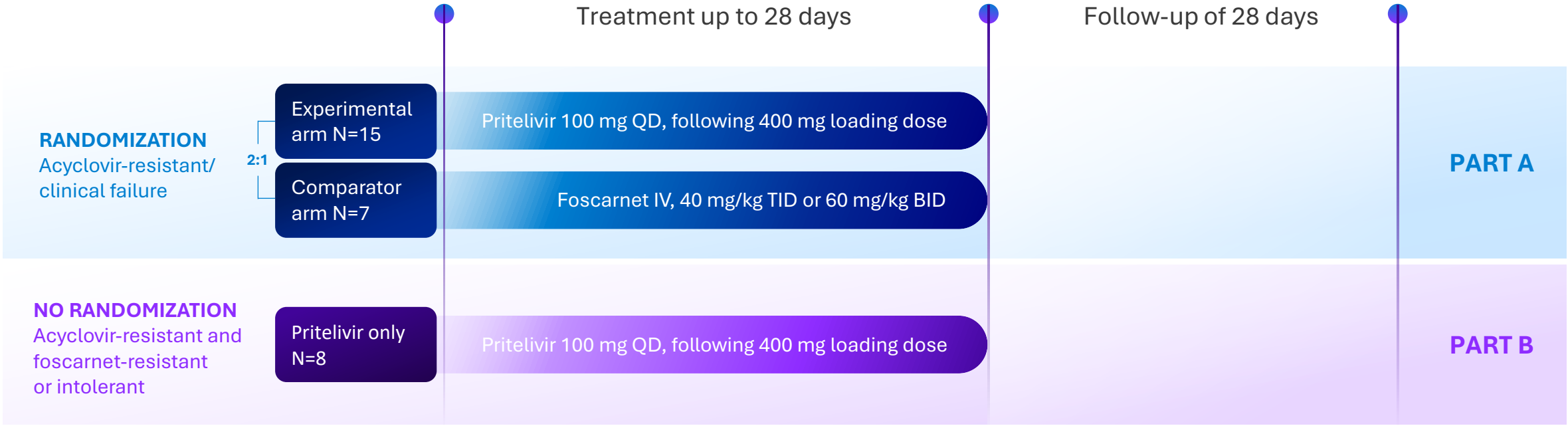
ClinicalTrials.gov ID NCT03073967

Sponsor AiCuris Anti-infective Cures AG

Information provided by AiCuris Anti-infective Cures AG (Responsible Party)

Trial Design AIC316-03-II-01 (PRIOH-1): Phase 2

Randomized, open-label, multi-center, comparator-controlled trial in immunocompromised ACV-resistant/refractory HSV patients



Pritelivir obtained FDA Breakthrough Therapy Designation (BTD)

Phase 2 data demonstrated higher healing rates and improved safety/tolerability in pritelivir treated patients

- **Higher healing rate observed** vs. foscarnet in acyclovir-resistant patients
- **Healing also seen in dual-resistant patients** with highest unmet need and no approved treatment options
- **Favorable safety and tolerability profile:**
  - Related AEs pritelivir 8.7% (2/23) vs. foscarnet 71.4% (5/7)
  - AE related discontinuations Part A: pritelivir 0% (0/15) vs. foscarnet 42.9% (3/7); Part B: 1/8 (12.5%)
- **Drug resistance rates** appeared to be lower with pritelivir (4.8% [1/21[1]]) than with foscarnet (20.0% [1/5[1]])

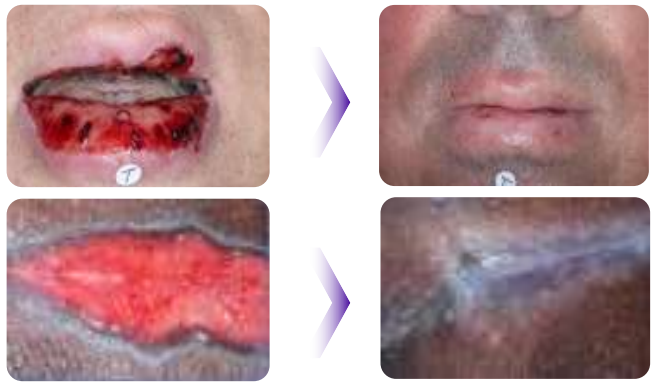
BREAKTHROUGH THERAPY

HEALING RATES (COMPLETE EPITHELIZATION OF MUCOCUTANEOUS HSV LESIONS)

Healing rates	Pritelivir	Foscarnet
PART A: acyclovir-resistant patients	**93%** (14/15 pts)	**57%** (4/7 pts)
PART B: Dual-resistant[2] patients	**63%** (5/8 pts)	N.A.

Data on file

ACYCLOVIR-RESISTANT INFECTION > AFTER PRITELIVIR TREATMENT

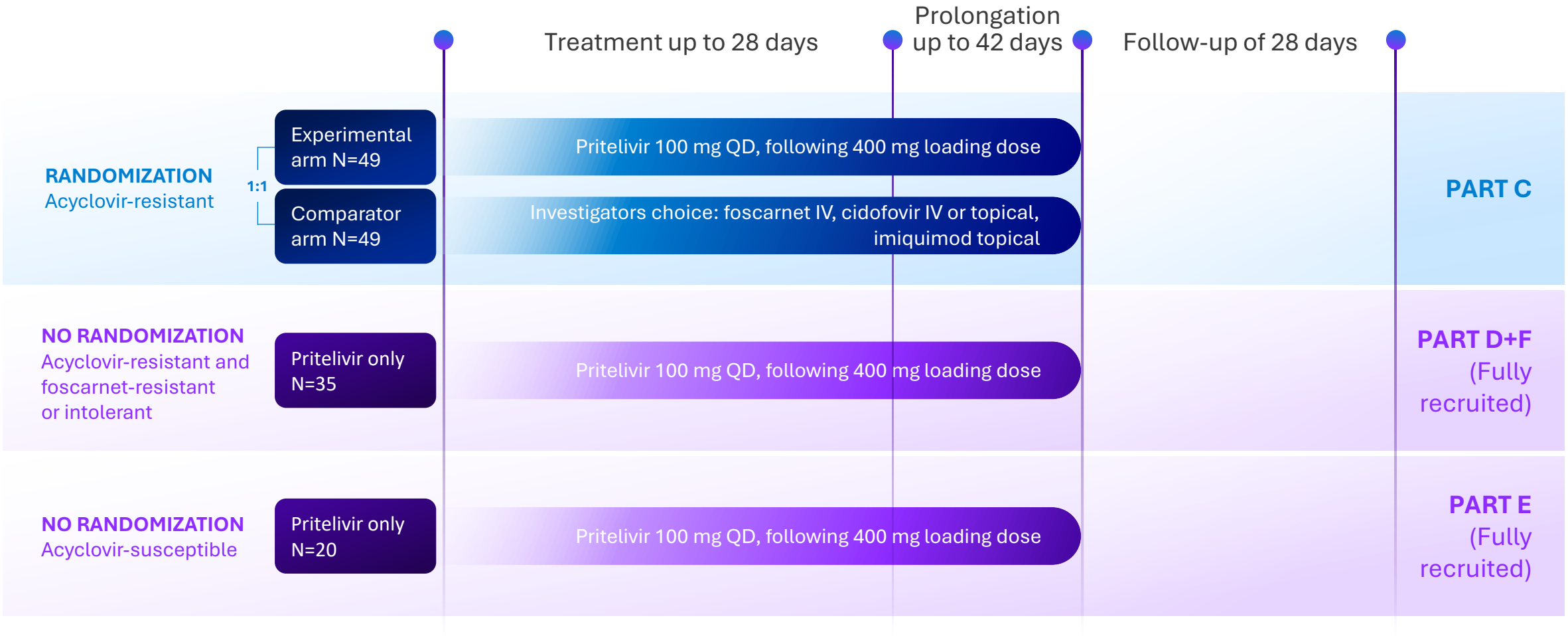


Workowski et al., Poster presentation, ID week 2021

[1]Denominator: number of subjects with post-treatment resistance testing
[2]Acyclovir-resistant and foscarnet-resistant and/or -intolerant

Trial Design AIC316-03-II-01 (PRIOH-1): Phase 3

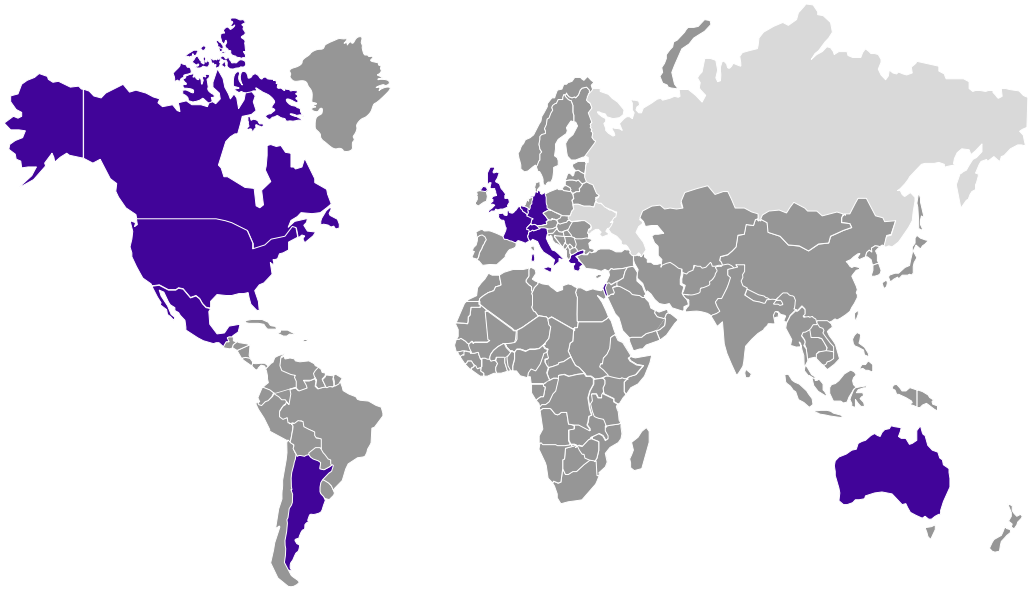
Randomized, open-label, multi-center trial in immunocompromised ACV-resistant/refractory HSV patients N=153



Pritelivir phase 3 trial is actively enrolling, aim for completion in 2025

NDA filing & approval planned in 2026

- **Randomized, open-label, multi-center trial** enrolling 153, mostly acyclovir-resistant, immunocompromised patients



- **Primary Endpoint:** healing rate (Day 28)
- **Secondary Endpoints:**
  - Efficacy endpoints includes healing rate (Day 42), time to lesion healing and cessation of shedding, pain scores, shedding rate, therapy failure rate, and resistance rate
  - Safety/tolerability endpoints includes AEs, SAEs, discontinuation, AEs of special interest, labs, ECGs, vital signs, discontinuation rates
  - PK and Quality of Life
- **Global study** with 60 sites in 14 countries

Trial AIC316-03-II-01 (PRIOH-1): Phase 3

German sites

ESSEN, GERMANY, 45147

Recruiting

Universitätsklinikum Essen

Contact: Oliver Witzke

004920172382413 anja.stemple@uk-essen.de

KÖLN, GERMANY, 50937

Recruiting

Universitätsklinikum Köln

Contact: Yasmin Habibullah

+4922147896287 Yasmin.habibullah@uk-koeln.de

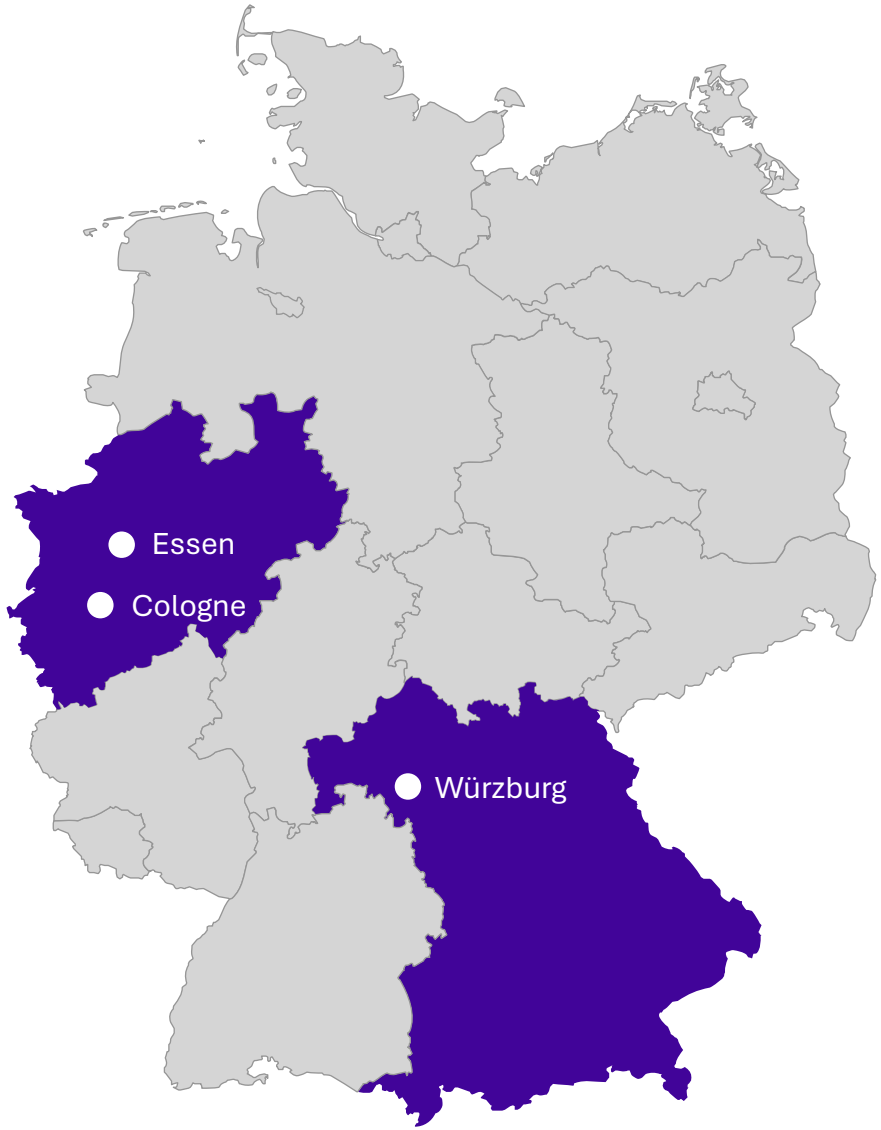
WÜRZBURG, GERMANY, 97080

Recruiting

Universitätsklinikum Würzburg

Contact: Cornelia Smidt

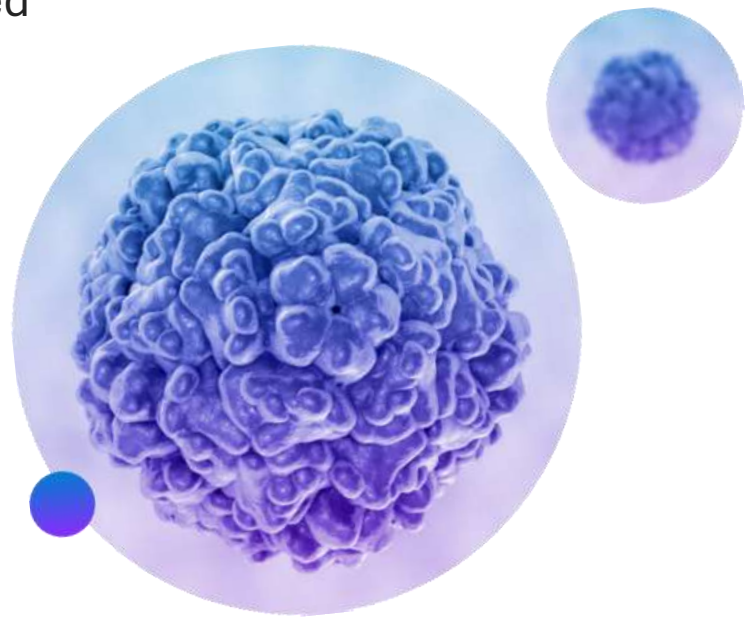
4993120144992 Smidt_C@ukw.de



Summary

Pritelivir for the treatment of resistant HSV infections

- A small molecule inhibitor of HSV-1 and HSV-2 replication targeting the viral helicase-primase complex
- Activity against nucleoside analog- and foscarnet-resistant HSV
- Prevents infection of uninfected cells, does not require activation by viral enzymes
- Statistically significant reduction in viral shedding and clinical lesions in otherwise healthy persons with genital HSV, superior to placebo and valacyclovir
- Treatment appeared to be safe and well tolerated in immunocompromised subjects with acyclovir resistant mucocutaneous HSV lesions
- A global Phase 3 trial in immunocompromised patients with resistant HSV infections and an Early Access Program are ongoing



aicuris

Thank you