Pritelivir, Novel Helicase Primase Inhibitor, Phase 3 Trial Results

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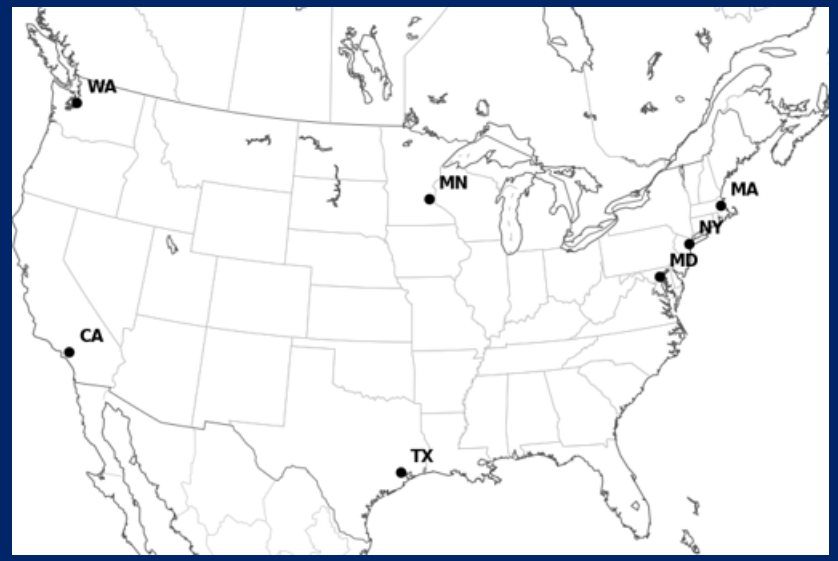
Treatment patterns and outcomes of refractory HSV in HCT: A multicenter real-world study

The HSV resistance working group of the TAVI forum

- Seven transplant centers in the USA, HCT from 2009-2024
- **Refractory HSV infection**: no clinical response after at least 7 days appropriately dosed anti-HSV antiviral(s)
- **Healing**: Full epithelialization of all lesions.
- **Follow up:** until healing or stopping HSV treatment

Participating Centers



The HSV Resistance Working Group of the TAVI forum

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Heavily immunosuppressed HCT recipients

	N=125 (%)
HSV prophylaxis at HSV diagnosis	125 (100)
Donor type	
-Mismatched/Haploidentical	63 (50.4)
T-cell depletion	37 (29.0)
Post-transplant cyclophosphamide	41 (32.8)
Relapse/Progression of malignancy	44 (35.2)
Corticosteroids at HSV diagnosis	57 (45.6)
Prednisone or equivalent ≥20mg/day	30 (24.0)
Absolute neutrophil count < 0.5 $X10^3/\mu L$	34 (27.2)
Platelet count <20$X10^3/\mu L$	38 (30.0)

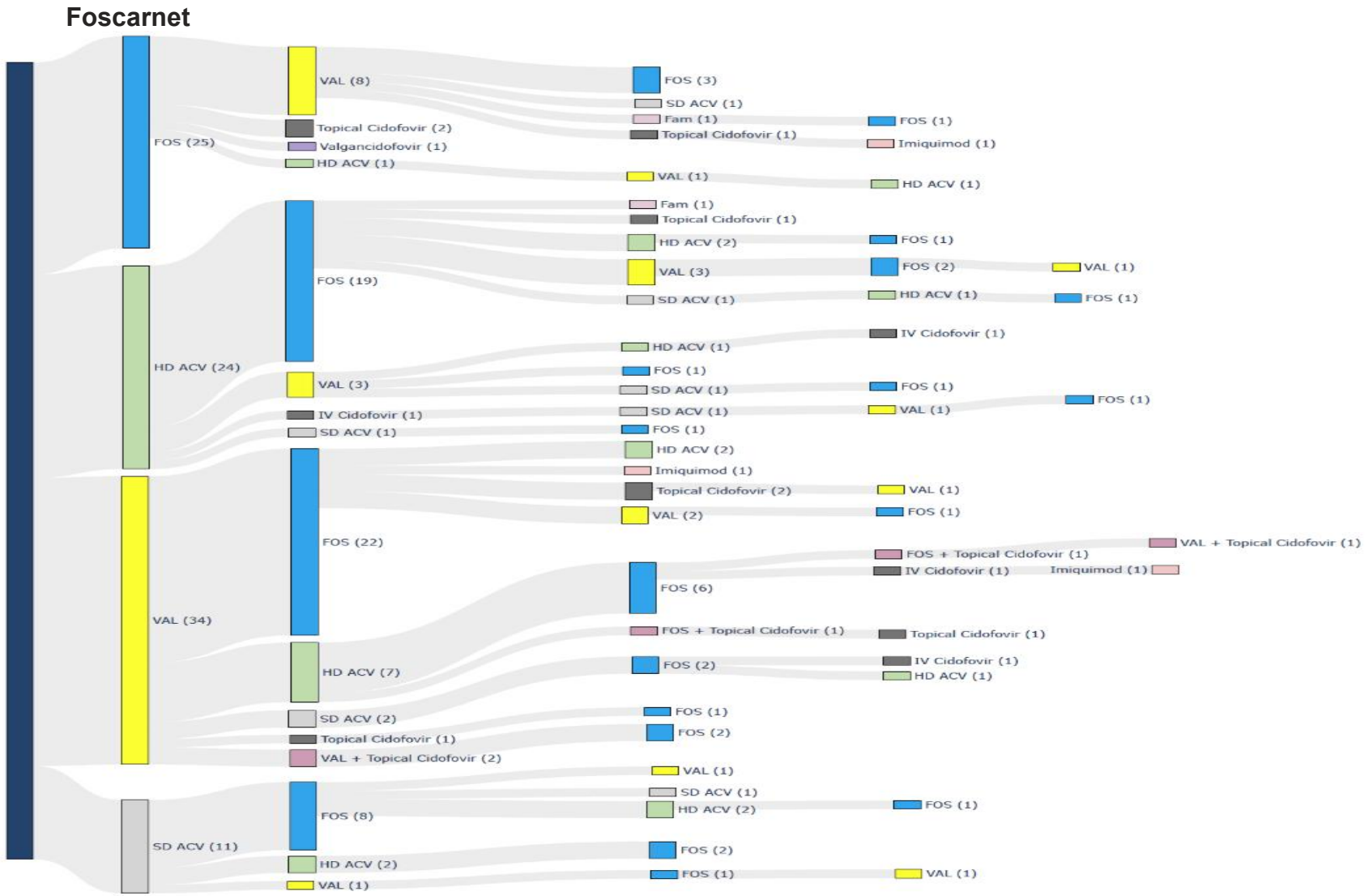
Foscarnet used in 75% of patients

Antiviral	No of patients[+]	No of courses	Total antiviral days	Mean[#] antiviral days (Range)
Foscarnet	**94**	**109**	**2,376 days**	**25.3 (3, 91)**
IV cidofovir	6	6	122 days	20.3 (7, 37)
Topical Cidofovir Imiquimod	21	28	1,147 days	54.6 (5, 154)

[+]Total 111 patients

*Courses with duration <2 days were removed. [#]Per patient for each antiviral for all treatment courses combined

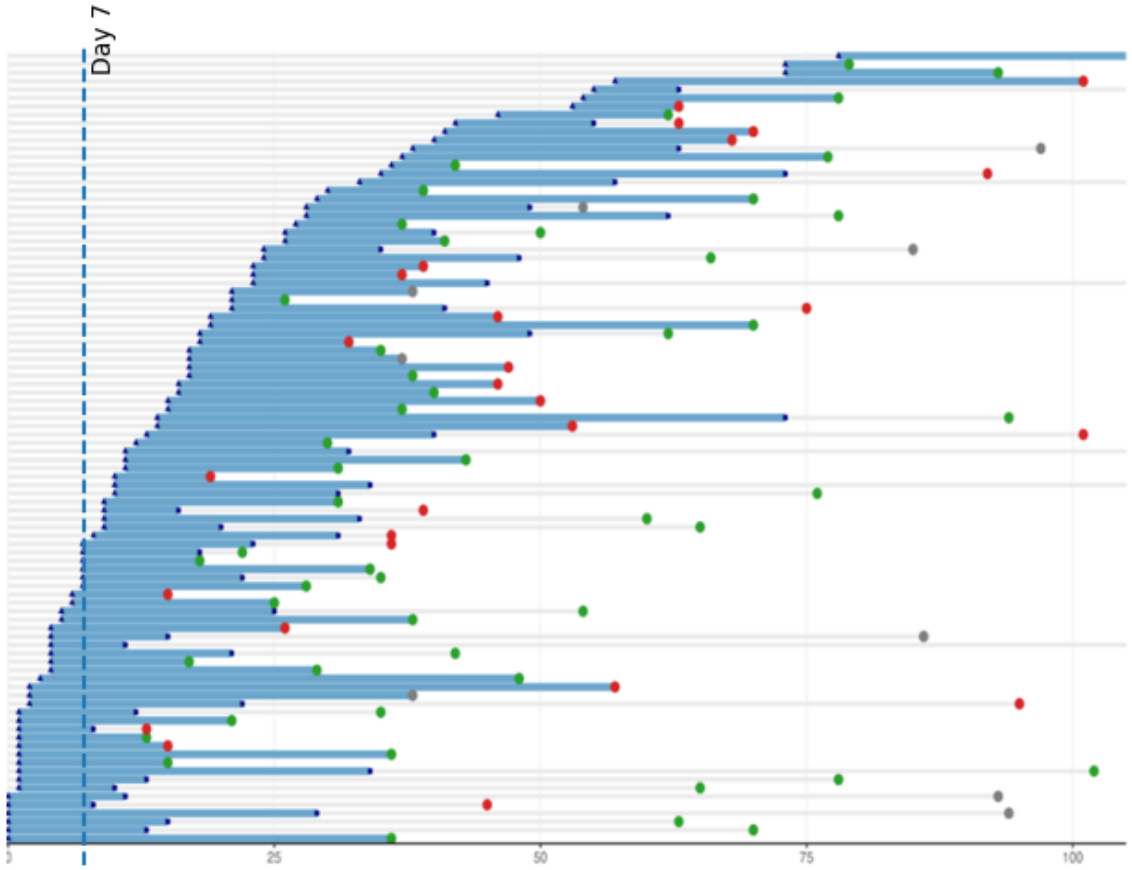
Complex and highly individualized regimens
94 patients treated with foscarnet



HSV
diagnosis

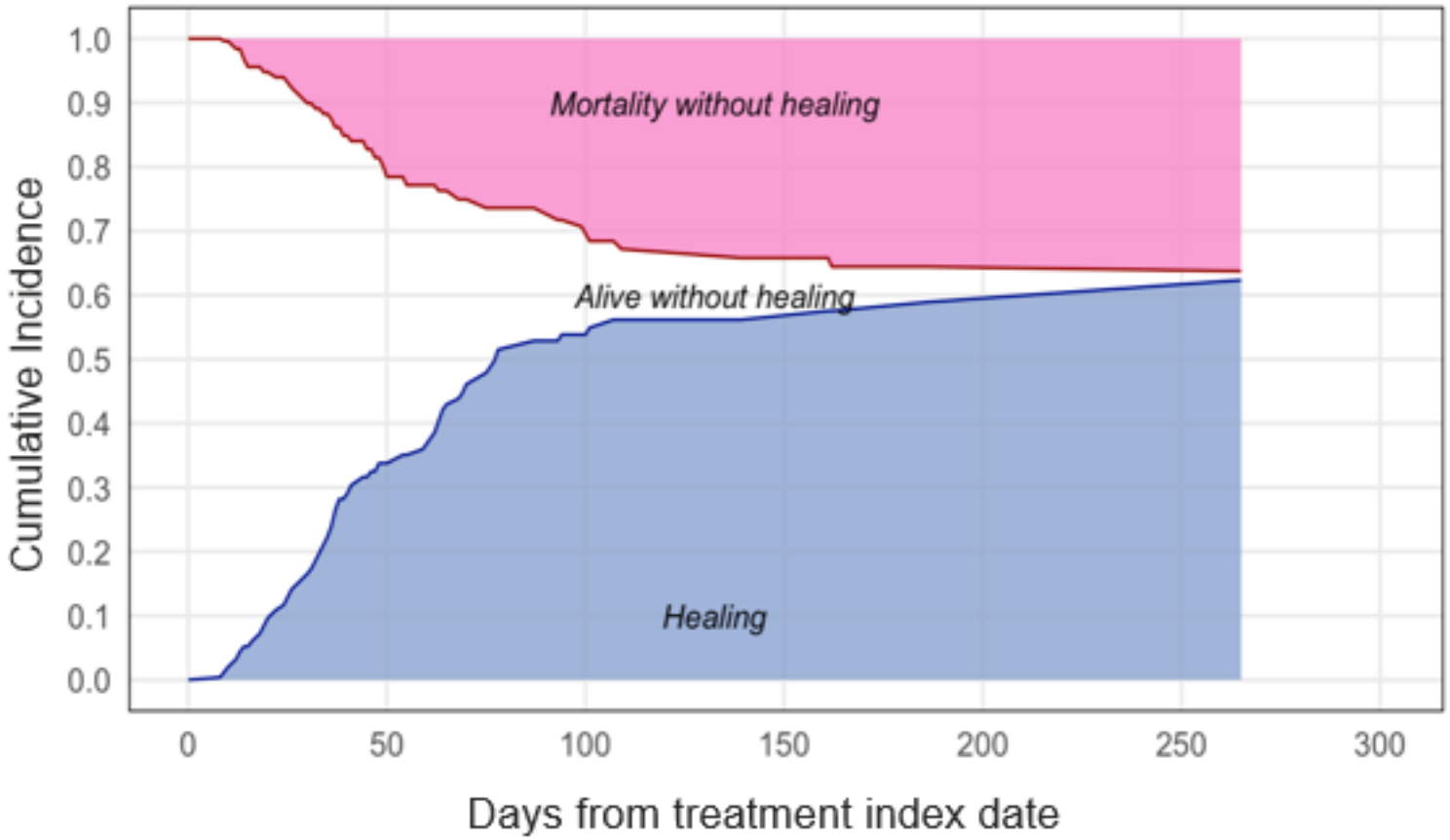
Sequential antiviral courses

62% patients started foscarnet >7 days from HSV diagnosis



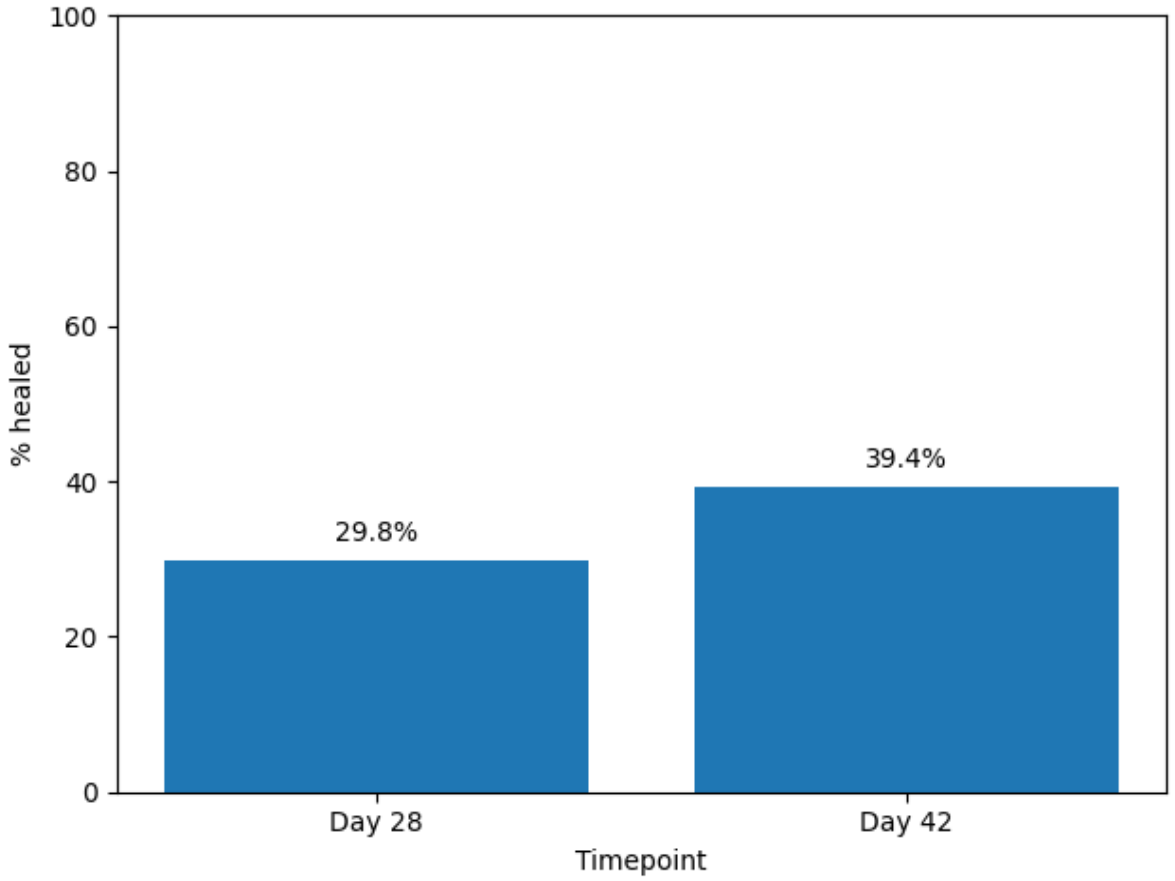
- Foscarnet started a median 11.5 days from HSV diagnosis (min 0 – max 78)
- Foscarnet treatment duration was a median 20 days (min 5 – max 91)

55% patients achieved complete healing



Median time to healing 38 days (Q1-Q3: 26, 65)

30% patients healed by Day 28 from start of foscarnet



Summary

- Heavily immunosuppressed HCT patients
- 55.2% patients healed after prolonged therapies, median 38 days
- 75% received foscarnet, renal toxicity reported in 40% of courses
- Unmet need for better therapies

Manuscript under review

7th Feb 2026: TANDEM late breaker oral presentation

Pritelivir demonstrated superior efficacy compared to investigator's choice treatment for refractory herpes simplex virus infections in immunocompromised patients: PRIOH-1, phase 3 safety and efficacy

Genovefa A. Papanicolaou presented on behalf of the PRIOH-1 investigators

Memorial Sloan Kettering Cancer Center and Weill Cornell Medical College, Cornell University, New York, USA.

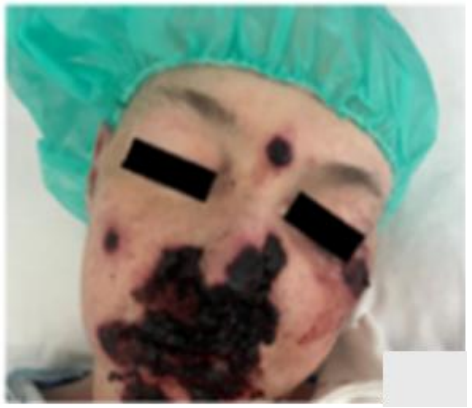
Clinical Burden of Refractory Herpes Simplex Virus Infection in Immunocompromised Patients

High unmet need for effective and well-tolerated treatment options

- Herpes simplex virus (HSV) infections: can be more frequent, prolonged, severe, and refractory leading to;
  - Increased hospitalisation rates
  - Risk of dissemination

- Aciclovir (ACV) resistance is not uncommon[1];
  - up to 14% in haematopoietic cell transplant (HCT) recipients
  - up to 3% in solid organ transplant (SOT) recipients
  - Between 3 - 7% in patients living with HIV (PLHIV)

- Treatment options for ACV-refractory patients are limited to foscarnet or 'off-label' medications (e.g. cidofovir and imiquimod)
  - Introduces administration burden (e.g. IV) and treatment limiting toxicities[2]



Adapted from Bussini et al.[3]

[1]Chemaly et al., *Clin Infect Dis*. 2925 Oct 6;81(3):593-601; [2]Hammond et al. *Open Forum Infect Dis*. 2024;11(3):ofae123; [3]Bussini L et al. *Clin Microbiology & Infection. 2025; 31(7): 1234-1236.*

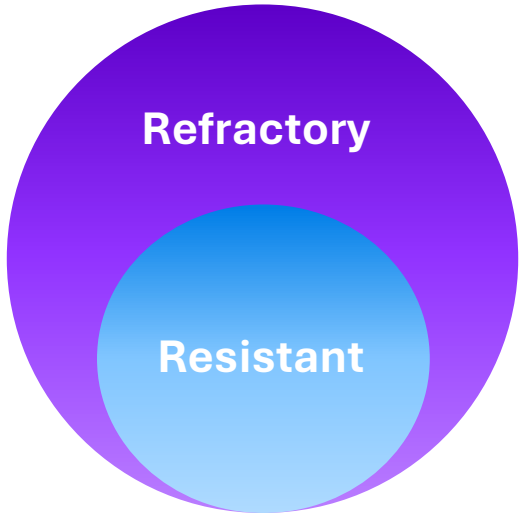
What Defines Refractory HSV Infection?

Refractory HSV

- No clinical improvement of HSV lesion(s) or new lesions after at least 7 days of standard-of-care HSV nucleoside analogue* treatment (excluding prophylaxis and suppressive therapy)

Resistant HSV

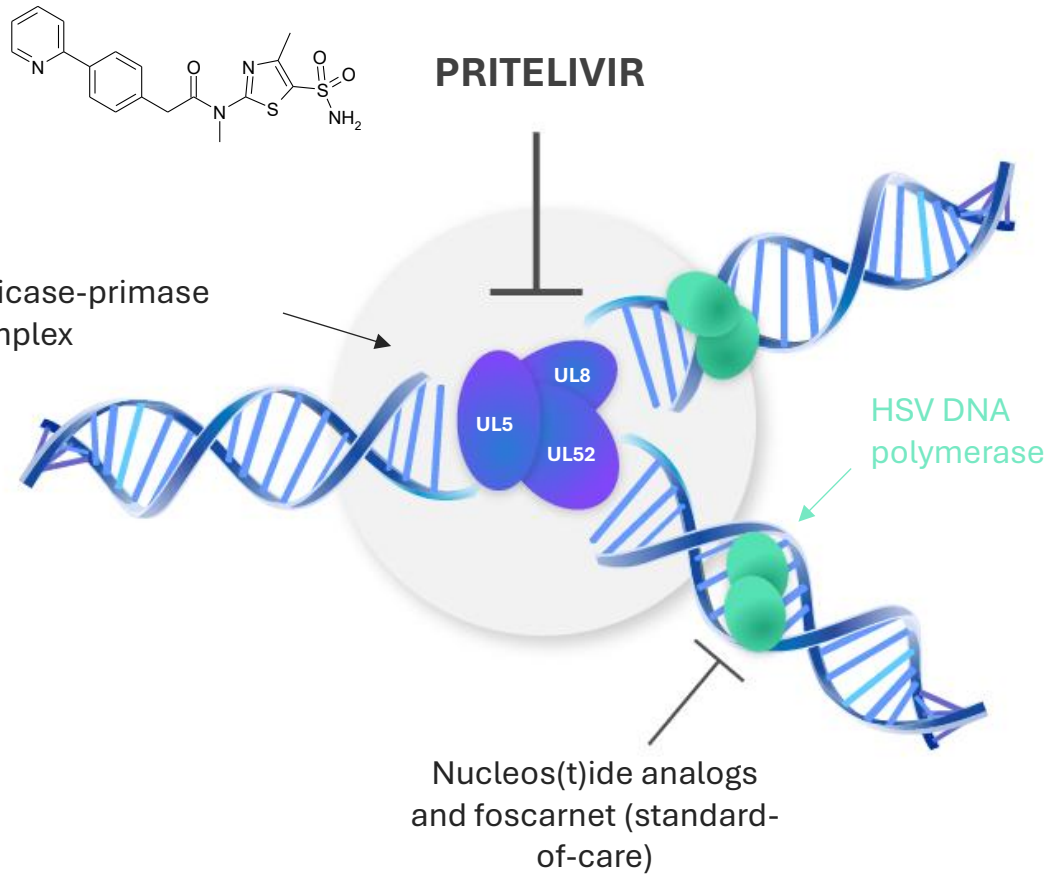
- A refractory HSV infection with laboratory-confirmed genotypic/phenotypic** resistance for the current HSV outbreak



*Therapeutic doses of nucleoside analogues include aciclovir (ACV), valaciclovir (VACV) or famciclovir (FCV).
**Genotypic: viral genetic alteration(s) that decreases susceptibility and/or phenotypic assay demonstrating increased IC50 above the assay cutoff to one or more antiviral drug(s).

[1]Chemaly et al., *Clin Infect Dis*. 2925 Oct 6;81(3):593-601.

Pritelivir is a Small Molecule with a Novel Mechanism of Action



- Pritelivir targets the viral helicase-primase complex[4,5]
- In contrast to existing drugs, pritelivir does not require activation by viral thymidine kinase, thus can prevent infection of uninfected cells
- Pritelivir is active against HSV-1 and HSV-2 isolates including nucleos(t)ide analog- and foscarnet-resistant isolates *in vitro*
- Pritelivir is orally bioavailable with a half-life of 60 hours allowing once-daily dosing
- Pritelivir has a low drug-drug interaction potential[6]

UL5 = helicase; UL52 = primase; UL8 = accessory protein

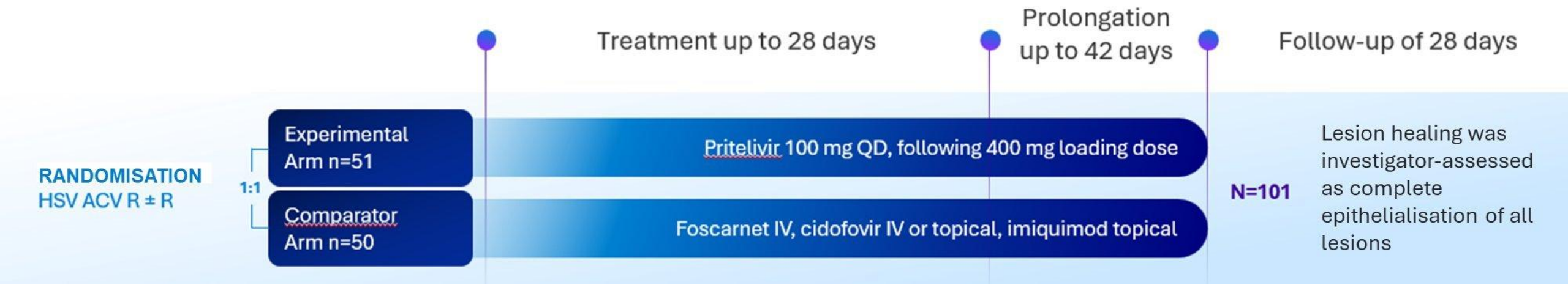
[4]Birkmann A, et al., *J Med Chem*. 2022; 65(20):13614-13628; [5]Birkmann A, Saunders R., *Antiviral Research*. 2025; 237:106152. [6]de Vries, et al., *Clinical Pharmacology in Drug Development* 13.7 (2024): 755-769.

Phase 3 PRIOH-1 Study Design

Randomised, open-label, multicentre trial

- **Study Aim:** To evaluate the efficacy and safety of pritelivir compared with investigator's choice treatment (ICT)
- **Primary endpoint:** % of patients with complete lesion healing (cure rate) up to 28 days of treatment
- **Secondary endpoints:** Include: safety and tolerability
- **Key inclusion criteria:** Immunocompromised adults with ACV refractory ± resistant (R±R)mucocutaneous HSV infection based on:
  - Refractory/Clinical Failure: No clinical improvement of HSV lesion(s) after ≥7 days with therapeutic doses of a nucleoside analogue*

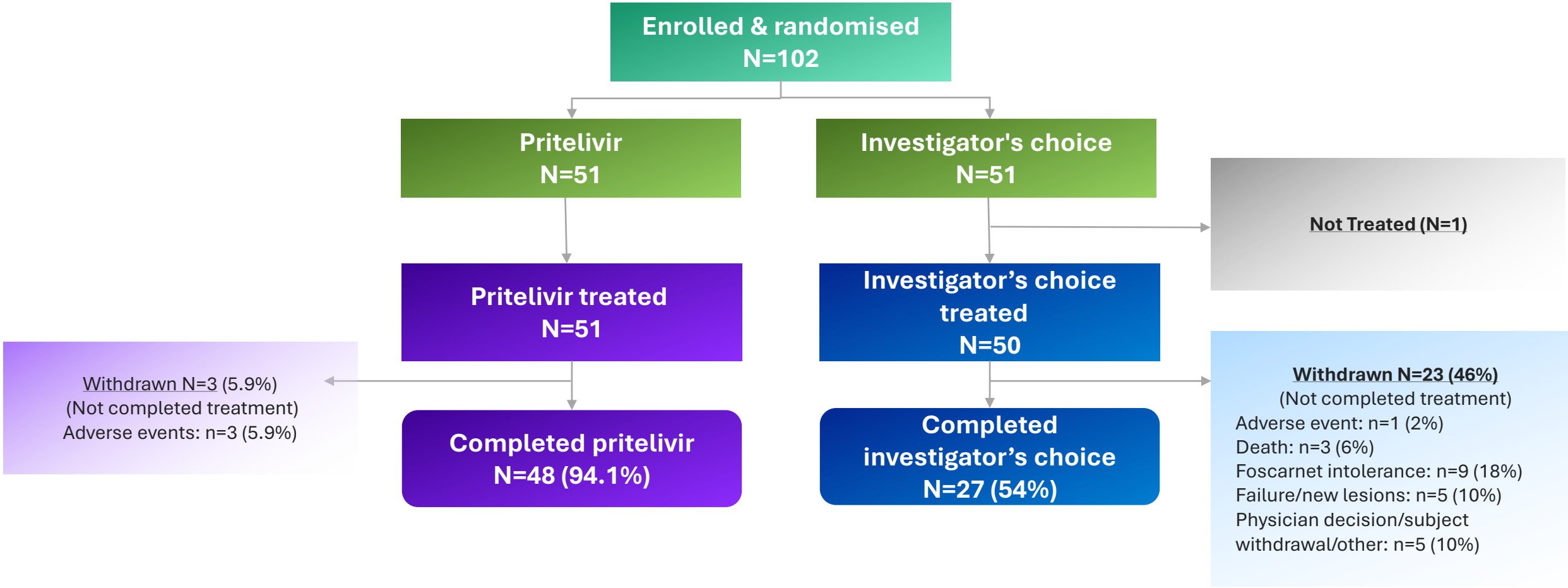
  OR
  - Resistance; Local laboratory-confirmed genotypic/phenotypic ACV resistance testing for current lesion



*Aciclovir, valaciclovir or famciclovir.

PRIOH-1: Patient Disposition

94% patients completed pritelivir vs 54% with investigator's choice treatment



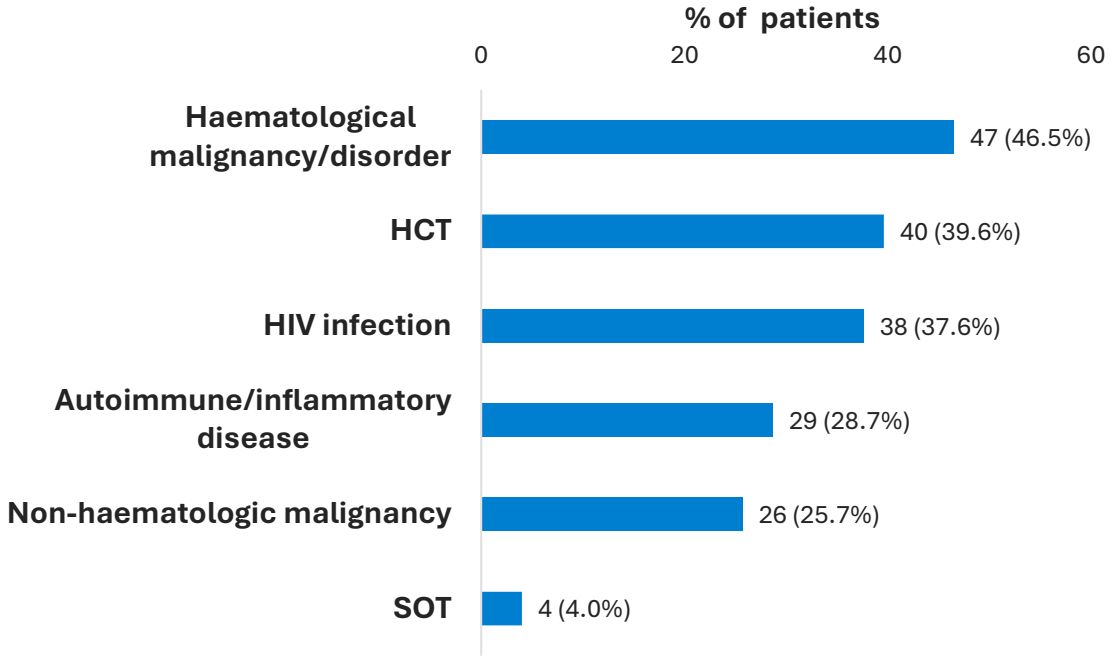
PRIOH-1 Demographics and Baseline Characteristics: 71% of Patients were Refractory

Full analysis set (FAS)	Pritelivir (N=51) n (%)	ICT (N=50) n (%)	Total (N=101) n (%)
Mean Age, years (SD)	49.2 (14.9)	56.0 (14.6)	52.6 (15.1)
Sex at birth			
Male	32 (62.7)	21 (42.0)	53 (52.5)
Female	19 (37.3)	29 (58.0)	48 (47.5)
Reason for Treatment start			
Refractory HSV (clinical failure)	39 (76.5)	33 (66.0)	72 (71.3)
Lab confirmed ACV-resistant	12 (23.5)	17 (34.0)	29 (28.7)
Race			
American Indian or Alaskan Native	11 (21.6)	5 (10.0)	16 (15.8)
Asian	1 (2.0)	2 (4.0)	3 (3.0)
Black or African American	14 (27.5)	9 (18.0)	23 (22.8)
White	20 (39.2)	29 (58.0)	49 (48.5)
Other	5 (9.8)	5 (10.0)	10 (9.9)
Length of Index Lesion (mm)			
n	47	42	89
Mean (SD)	31.2 (28.3)	37.3 (41.7)	34.1 (35.2)

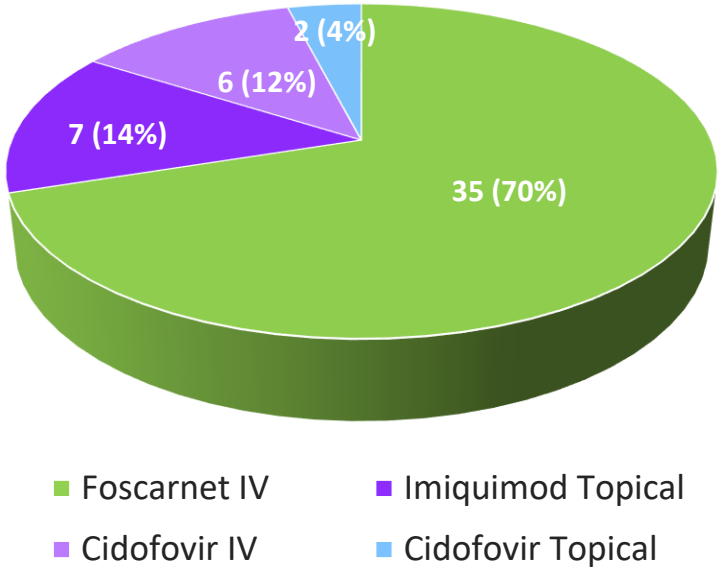
Baseline is defined as the last valid measurement prior to the first dose of the study medication. Local lab ACV-R test results - local lab Positive genotypic/phenotypic ACV resistance testing for current lesion.

PRIOH-1 Baseline Characteristics: Underlying Immunocompromised Condition & Distribution of Investigator's Choice Treatment

Underlying disease: overall population (FAS)* (N=101) n (%)

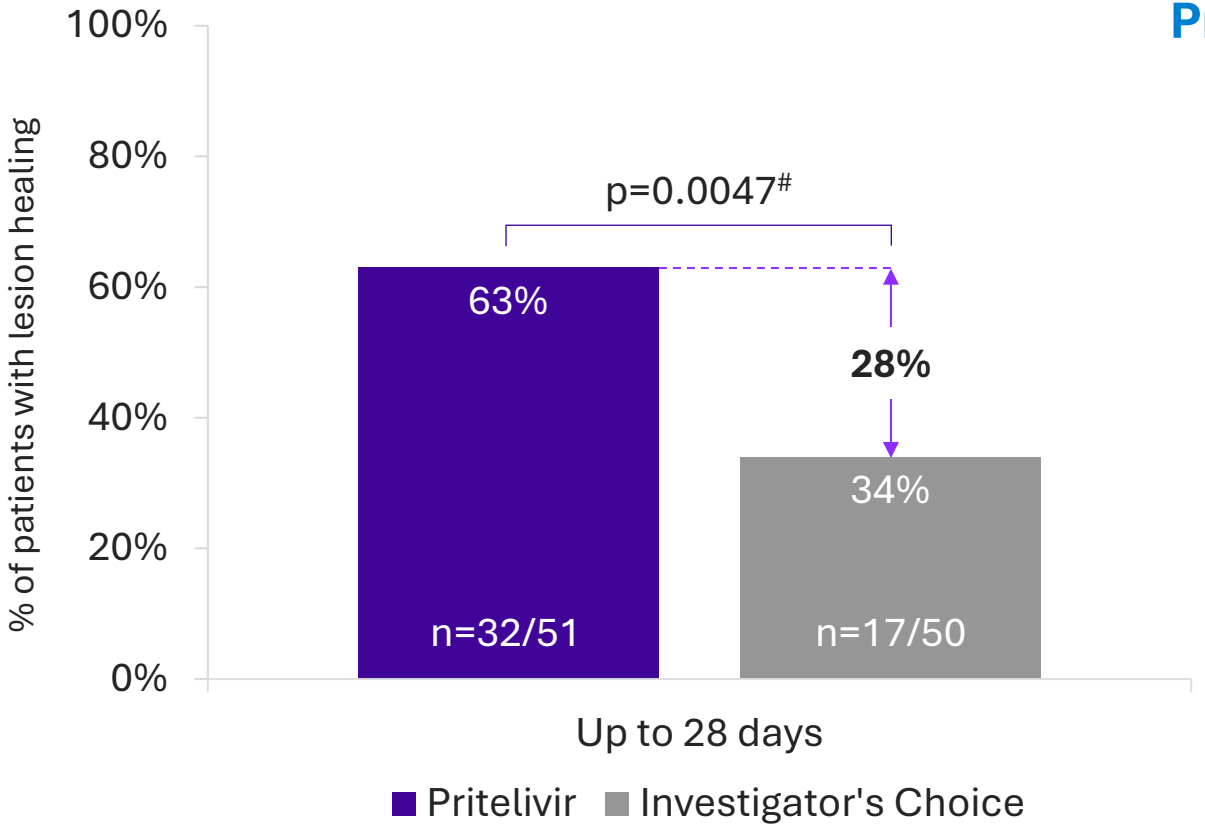


Investigator's choice treatment: overall population (N=50) n (%)



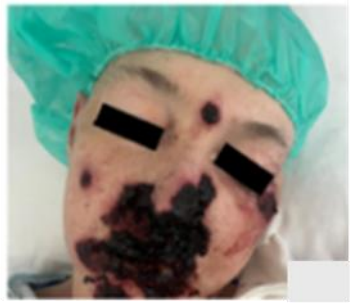
*Patients may have more than one underlying condition; each subject is counted once under each applicable 'Underlying Disease' category. Baseline is defined as the last valid measurement prior to the first dose of the study medication.

Pritelivir Demonstrated Superior Efficacy Compared to Investigator's Choice Treatment

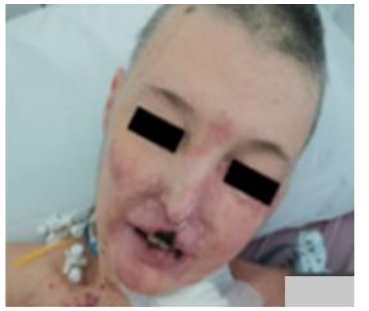


Pritelivir met its phase 3 primary endpoint (FAS)

- Pritelivir achieved a statistically significant higher rate of complete lesion healing (62.7%) vs ICT (34%), up to 28 days of treatment; adjusted treatment difference 28.4% (95% CI, 9.6-47.3); p=0.0047



Before pritelivir treatment



After 27 days of pritelivir treatment

Adapted from Bussini et al.

PRIOH-1: Pritelivir Demonstrated a Favourable Safety and Tolerability Profile

Lower rates of drug-related TEAE discontinuations on pritelivir (2%) vs ICT(20%)

Safety population	Pritelivir (N=51) n (%)	ICT (N=50) n (%)
Patients with any TEAE	41 (80.4)	45 (90.0)
Exposure-Adjusted Event Rate per patient year	42.8	102.0
Drug-Related TEAEs	**11 (21.6)**	**27 (54.0)**
Treatment-Emergent Serious Adverse Events	10 (19.6)	15 (30.0)
Treatment Discontinuation due to any TEAE	2 (3.9)	11 (22.0)
Treatment Discontinuation due to Drug-Related TEAEs	**1 (2.0)**	**10 (20.0)**
Patients with any TEAEs of Special Interest	13 (25.5)	27 (54.0)
Skin Disorders	5 (9.8)	8 (16.0)
Haematological AE	5 (9.8)	14 (28.0)
Renal/Urinary Disorders	3 (5.9)	13 (26.0)
Electrolyte Abnormalities	1 (2.0)	8 (16.0)

PRIOH-1: Fewer TEAEs with Pritelivir vs Investigator's Choice Treatment (Incidence of TEAEs ≥5%)

MedDRA preferred term	Pritelivir (N=51) n (%)	ICT (N=50) n (%)
Nausea	4 (7.8)	12 (24.0)
Diarrhoea	6 (11.8)	7 (14.0)
Headache	7 (13.7)	6 (12.0)
Vomiting	3 (5.9)	5 (10.0)
Dizziness	3 (5.9)	4 (8.0)
Hypokalaemia	0	7 (14.0)
Hypomagnesaemia	1 (2.0)	6 (12.0)
Thrombocytopenia	1 (2.0)	6 (12.0)
Anaemia	1 (2.0)	4 (8.0)
Cough	2 (3.9)	3 (6.0)
Decreased Appetite	4 (7.8)	1 (2.0)

MedDRA, medical dictionary for regulatory activities

Conclusions

- Pritelivir is a novel oral helicase-primase inhibitor that retains activity against nucleo(t)side analog- and foscarnet-resistant HSV-1 and HSV-2 isolates *in vitro*
- PRIOH-1 phase 3 trial met the primary endpoint of complete lesion healing up to 28 days of treatment; demonstrating superior efficacy compared with ICT in immunocompromised patients with R±R HSV infection
- Pritelivir showed a favourable safety and tolerability profile compared to ICT, which are limited by toxicity and/or administration burden
- Discontinuation rates and drug-related TEAEs were higher for ICT than for pritelivir treated patients
- Pritelivir is a promising oral agent to address the significant unmet need in the treatment of ACV-refractory ± resistant HSV infections in immunocompromised patients