

Treatment of Herpes Simplex Encephalitis with the Helicase-Primase Inhibitor Pritelivir in an Immunocompromised Patient

Catherina Lueck¹, Christina Rautenberg¹, Alexander Birkmann², Susanne Bonsmann², Alessandra Marini², Melanie Sumner², Thomas Schroeder¹, Sebastian Voigt³

¹ Department of Haematology and Stem Cell Transplantation, West German Cancer Center, University Hospital of Essen, Essen, Germany

² AiCuris Anti-Infective Cures AG, Friedrich-Ebert-Str. 475, 42117 Wuppertal, Germany

³ Institute for Virology, University Hospital Essen, University of Duisburg-Essen, Essen, Germany



SUMMARY

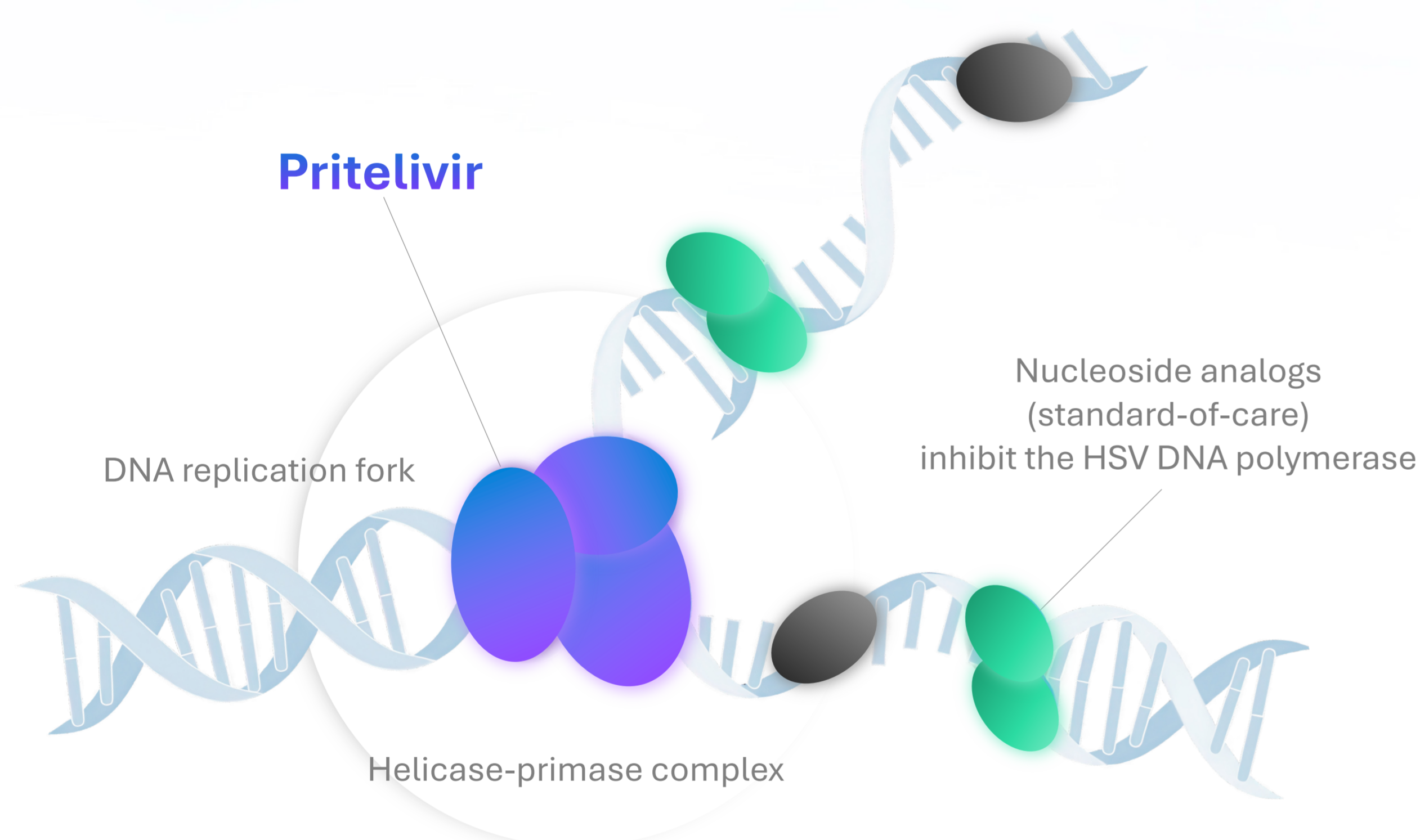
Herpes simplex encephalitis (HSE) is a rare but serious viral infection of the central nervous system, particularly dangerous in immunocompromised patients. This case report describes the first clinical use of pritelivir, a novel helicase primase inhibitor, in the treatment of refractory HSE. The patient, a 49-year-old immunocompromised man who had undergone hematopoietic cell transplantation, initially responded to treatment with acyclovir or foscarnet but experienced worsening symptoms and progredient edema and cerebral necrosis in MR imaging. Combined pritelivir and acyclovir therapy was initiated under a compassionate use program.

The addition of pritelivir was followed by a significant reduction in cerebrospinal fluid (CSF) HSV-1 viral load to undetectable levels, clinical improvement and stabilization of neurological symptoms. The drug was well tolerated, with plasma and CSF concentrations above the effective antiviral threshold.

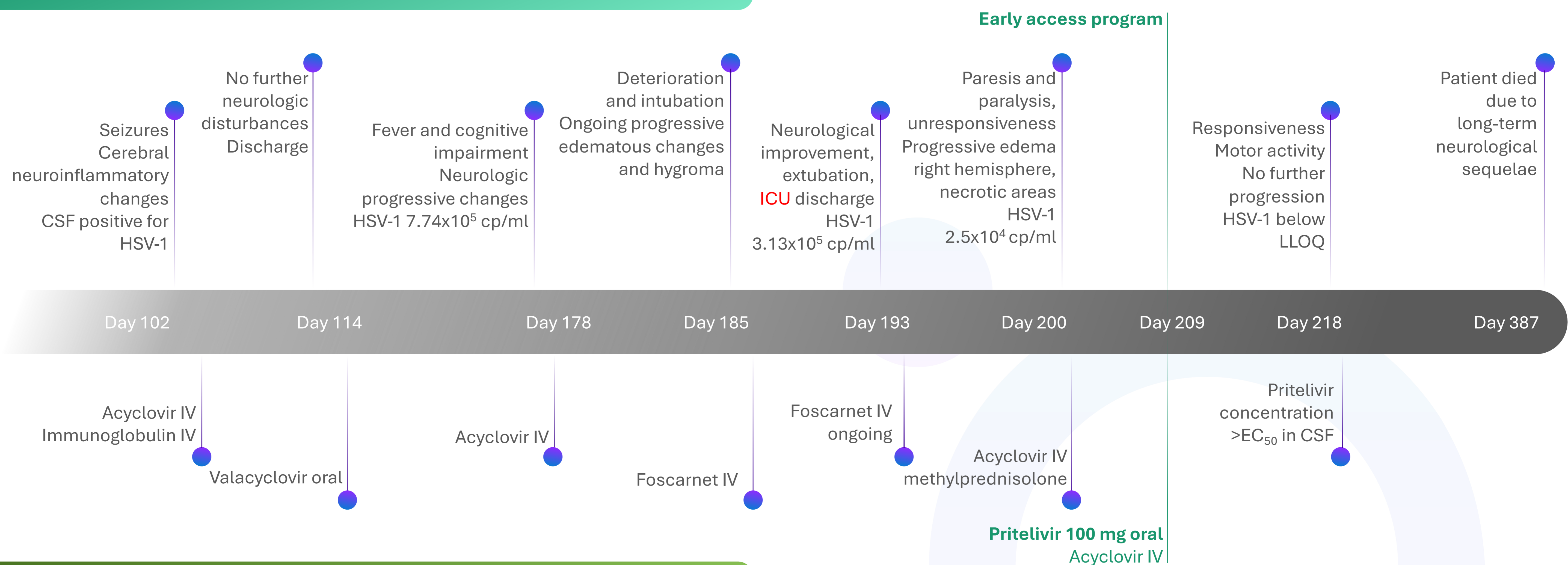
This case highlights the potential of pritelivir as a treatment option for refractory HSE in immunocompromised patients, although further studies are needed to confirm its efficacy and explore the benefits of earlier intervention.

PRITELIVIR IS A SMALL MOLECULE WITH A NOVEL MECHANISM OF ACTION

Pritelivir inhibits the viral helicase-primase complex



CLINICAL COURSE



CONCLUSION

- This is the first documented clinical case of pritelivir in treatment-refractory HSE
- It highlights the potential of pritelivir for treatment of HSE, particularly in immunocompromised patients with refractory infection
- During pritelivir treatment motor activity and responsiveness of the patient improved with HSV-1 being below lower limits of quantification
- Further clinical data is needed to elucidate if earlier intervention could prevent long term neurological sequelae

PRITELIVIR IS A SMALL MOLECULE WITH A NOVEL MECHANISM OF ACTION

- Small molecule inhibiting viral replication of HSV-1 and HSV-2
- Targets the viral helicase-primase complex
- Prevents infection of uninfected cells, no activation by viral enzymes required
- Pritelivir orally bioavailable with a long half-life allowing once-daily dosing
- Active against nucleoside analog and foscarnet resistant HSV
- Significant reduction in viral shedding and clinical lesions shown in immunocompetent individuals with genital HSV, superior to valacyclovir
- Treatment appeared to be safe and well tolerated in immunocompromised subjects with acyclovir resistant mucocutaneous HSV lesions
- Global Phase 3 trial in immunocompromised patients with resistant HSV infections and an Early Access Program ongoing

HERPES SIMPLEX ENCEPHALITIS IN IMMUNOCOMPROMISED PATIENTS

- Acute herpes simplex encephalitis (HSE) is a rare disease with an incidence of 0.2-0.3/100.000/year
- HSE has a lethality of approximately 30% despite adequate treatment and causes permanent neurological damage in up to 70% of cases
- Recipients of allogeneic hematopoietic cell transplantation (HCT) are at high risk of HSV reactivation causing HSE in approximately 0.1% to 1.8% of all HCT recipients
- Standard treatment for HSE is high-dose acyclovir IV with 10 mg/kg TID
- In case of clinical or laboratory proven acyclovir resistance, foscarnet serves as alternative with effective cerebral spinal fluid (CSF) penetration

THE CASE

- 49-year-old male 100 days after HCT for acute myeloid leukemia with good hematological engraftment and without any signs of acute graft-versus-host disease
- Immunosuppressive treatment with anti-thymocyte globulin, tacrolimus and mycophenolate mofetil peri-transplant