PATHOGEN PROFILE
PEER REVIEWED

Feline Herpesvirus Type 1

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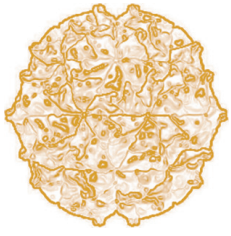

Sketch of structure as depicted by University of California, Riverside laboratory

Famciclovir

Dose: Ideal dose still being established and its safety investigated

Option: 90 mg/kg PO q8h associated with significant improvement in cats with experimental primary herpetic disease[1]

Option: 40 mg/kg PO q8h produced plasma penciclovir concentrations similar to those achieved with above dose[2]
- Also produced tear penciclovir concentrations likely effective against feline herpesvirus type 1 (FHV-1)[3]

Famciclovir is a prodrug that must be converted to its active metabolite penciclovir, a purine analog with in vitro efficacy against FHV-1.[4-6] Because cats are markedly deficient in the enzyme required for this conversion,[7] famciclovir metabolism is limited and nonlinear.[1,2]

Lysine

Dose: 500 mg PO q12h[8]
- Must be administered as twice-daily bolus
- Unsuccessful when 250 or 500 mg administered only once daily to shelter cats[9] and when patients permitted ad lib access to diet fortified with lysine[10,11]

Lysine limits in vitro replication of FHV-1 at high concentrations and with concurrent depletion of arginine[12]; however, this effect was not seen in media containing physiologic lysine and arginine concentrations.[13] In experimental conditions, lysine supplementation may reduce viral shedding in cats latently infected with FHV-1[14] and clinical signs in cats undergoing primary exposure.[8]

Cidofovir

Dose: 1 drop of 0.5% ophthalmic solution to affected eye q12h[15]
- Do not administer systemically.

Cidofovir is a cytosine analog that creates metabolites with a relatively long tissue half-life, permitting it to be used less frequently than other antiviral drugs[16]; when applied topically to cats experimentally infected with FHV-1, cidofovir reduced viral shedding and clinical disease.[15]

Reports showed that cidofovir can be associated with stenosis of the nasolacrimal drainage system components during experimental topical use in humans and rabbits,[17,18] but this adverse effect has not been noted in cats.

Trifluridine

Dose: 1 drop of 1% ophthalmic solution to affected eye at least 5 times daily[19]
- Do not administer systemically.

Trifluridine is a thymidine analog with in vitro efficacy against FHV-1[20] and excellent corneal epithelial penetration.[21] It often is

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not well tolerated by cats, likely because of a stinging reaction also reported in humans; no controlled studies assessing its use in cats have been conducted.

Idoxuridine

Dose: In United States, can be obtained from compounding pharmacists only; following forms recommended (do not administer systemically)

Compounded form: 1 drop of 0.1% ophthalmic solution to affected eye at least 5 times daily[19]

Compounded form: 1/4-inch strip of 0.5% ophthalmic ointment to affected eye at least 5 times daily[19]

Like trifluridine, idoxuridine is a thymidine analog with in vitro efficacy against FHV-1.[4,20] It was commercially available as an ophthalmic solution or ointment for humans with disease attributable to herpes simplex virus type 1 (HSV-1), is well tolerated by most cats, and seems efficacious in many; however, no controlled studies assessing its use in cats have been conducted.

Vidarabine

Dose: In United States, can be obtained from compounding pharmacists only; following form recommended (do not administer systemically)

Compounded form: 1/4-inch strip of 3% ophthalmic ointment to affected eye at least 5 times daily[19]

Vidarabine, an adenosine analog with in vitro efficacy against FHV-1,[20] affects a different viral replication step than do trifluridine and idoxuridine and thus may be effective in patients with a disease apparently resistant to these drugs; no controlled studies in cats have been conducted.

Acyclovir

Dose: 1/4-inch strip of 0.5% ophthalmic ointment to affected eye at least 5 times daily; not available in the United States[22]

Acyclovir is a purine analog with relatively low in vitro potency against FHV-1[4,20,22] and poor absorption following oral administration.[23] It is also associated with nephrotoxicity and bone marrow suppression[22]; therefore, systemic administration is not recommended in cats.

Cats treated topically 5 times daily with acyclovir ophthalmic ointment experienced a median time of 12 days to resolution of clinical signs,[22] whereas resolution in cats treated q8h took approximately twice as long and occurred only when therapy was increased to 5 times daily. Toxicity was not seen with topical application.[22]

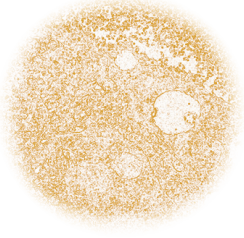
Valacyclovir

Dose: Use contraindicated in cats

When applied topically to cats experimentally infected with FHV-1, cidofovir reduced viral shedding and clinical disease.[15]

FHV-1 = feline herpesvirus type 1

Based on current safety and efficacy evidence, the optimal therapy is oral famciclovir 3 times daily.[1-3]



FHV-1 = feline herpesvirus type 1

Valacyclovir, an acyclovir prodrug, enhances acyclovir bioavailability, thereby increasing plasma acyclovir concentrations in cats to levels associated with bone marrow suppression and fatal hepatic and renal necrosis.[24] Valacyclovir should never be administered systemically to cats.

Ganciclovir

Dose: No data available for cats

- In humans, available for systemic (IV, PO), intravitreal, and topical ophthalmic (0.15% gel) administration

Ganciclovir, a purine analog, appears to be at least 10-fold more effective against FHV-1 than is acyclovir.[4,25] However, in humans this agent is relatively more toxic than other antivirals, and there are no reports on its safety or efficacy in cats; thus, it should not be used systemically in cats at this stage. There are no reports of its topical use in cats.

Closing Remarks

Based on current evidence for safety and efficacy of antiviral drugs in cats infected with FHV-1, optimal therapy appears to be famciclovir given orally 3 times daily.[1-3]

- If topical therapy is preferred and owners can administer drugs frequently, then topical idoxuridine is usually well tolerated and often effective.[4,20]
- For owners who cannot manage therapy more often than q12h, the only topical antiviral with proven efficacy is cidofovir.[15,16]
- Lysine can be useful adjunct therapy in some patients, especially to reduce frequency and severity of recrudescent disease episodes.[8-11,14]
  - —Must be administered q12h, not ad lib with food

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REFERENCES

1. **Evaluation of orally administered famciclovir in cats experimentally infected with feline herpesvirus type-1.** Thomasy SM, Lim CC, Reilly CM, et al. *Am J Vet Res* 72(1):85-95, 2011.
2. **Pharmacokinetics of penciclovir in healthy cats following oral administration of famciclovir or intravenous infusion of penciclovir.** Thomasy SM, Whittem T, Bales JL, et al. *Am J Vet Res* 73(7):1092-1099, 2012.
3. **Pharmacokinetics of famciclovir and penciclovir in tears following oral administration of famciclovir to cats: A pilot study.** Thomasy SM, Covert JC, Stanley SD, Maggs DJ. *Vet Ophthalmol* 15(5):299-306, 2012.
4. **In vitro efficacy of ganciclovir, cidofovir, penciclovir, foscarnet, idoxuridine, and acyclovir against feline herpesvirus type-1.** Maggs DJ, Clarke HE. *Am J Vet Res* 65(4):399-403, 2004.
5. **Penciclovir is a potent inhibitor of feline herpesvirus-1 with susceptibility determined at the level of virus-encoded thymidine kinase.** Hussein IT, Menashy RV, Field HJ. *Antiviral Res* 78(3):268-274, 2008.
6. **Development of a quantitative real-time TaqMan PCR assay for testing the susceptibility of feline herpesvirus-1 to antiviral compounds.** Hussein IT, Field HJ. *J Virol Methods* 152(1-2):85-90, 2008.
7. **Identification of aldehyde oxidase as the neonicotinoid nitroreductase.** Dick RA, Kanne DB, Casida JE. *Chem Res Toxicol* 18(2):317-323, 2005.
8. **Effect of oral administration of L-lysine on conjunctivitis caused by feline herpesvirus in cats.** Stiles J, Townsend WM, Rogers QR, Krohne SG. *Am J Vet Res* 63(1):99-103, 2002.
9. **Oral supplementation with L-lysine did not prevent upper respiratory infection in a shelter population of cats.** Rees TM, Lubinski JL. *J Feline*

Med Surg 10(5):510-513, 2008.
10. **Effects of dietary lysine supplementation on upper respiratory and ocular disease and detection of infectious organisms in cats within an animal shelter.** Drazenovich TL, Fascetti AJ, Westermeyer HD, et al. *Am J Vet Res* 70(11):1391-1400, 2009.
11. **Effects of dietary lysine supplementation in cats with enzootic upper respiratory disease.** Maggs DJ, Sykes JE, Clarke HE, et al. *J Feline Med Surg* 9(2):97-108, 2007.
12. **Effects of L-lysine and L-arginine on in vitro replication of feline herpesvirus type-1.** Maggs DJ, Collins BK, Thorne JG, Nasisse MP. *Am J Vet Res* 61(12): 1474-1478, 2000.
13. **Effects of physiologic concentrations of l-lysine on in vitro replication of feline herpesvirus 1.** Cave NJ, Dennis K, Gopakumar G, Dunowska M. *Am J Vet Res* 75(6):572-580, 2014.
14. **Efficacy of oral supplementation with L-lysine in cats latently infected with feline herpesvirus.** Maggs DJ, Nasisse MP, Kass PH. *Am J Vet Res* 64(1):37-42, 2003.
15. **Effect of topical ophthalmic application of cidofovir on experimentally induced primary ocular feline herpesvirus-1 infection in cats.** Fontenelle JP, Powell CC, Veir JK, et al. *Am J Vet Res* 69(2):289-293, 2008.
16. **Particular characteristics of the anti-human cytomegalovirus activity of (S)-1-(3-hydroxy-2-phosphonyl methoxypropyl)cytosine (HPMPC) in vitro.** Neyts J, Snoeck R, Balzarini J, De Clercq E. *Antiviral Res* 16(1):41-52, 1991.
17. **Treatment of conjunctival squamous cell carcinoma with topical cidofovir.** Sherman MD, Feldman KA, Farahmand SM, Margolis TP. *Am J Ophthalmol* 134(3):432-433, 2002.
18. **Clinical evaluation of local ocular toxicity in candidate anti-adenoviral agents in vivo.** Inoue H, Sonoda KH, Ishikawa M, et al. *Ophthalmologica* 223(4):233-238, 2009.
19. **Antiviral therapy for feline herpesvirus infections.** Maggs DJ. *Vet Clin North Am Small Anim Pract* 40(6):1055-1062, 2010.
20. **In vitro susceptibility of feline herpesvirus-1 to vidarabine, idoxuridine, trifluridine, acyclovir, or bromovinyldeoxyuridine.** Nasisse MP, Guy JS, Davidson MG, et al. *Am J Vet Res* 50(1):158-160, 1989.
21. **Intraocular penetration of trifluridine.** Pavan-Langston D, Nelson DJ. *Am J Ophthalmol* 87(6):814-818, 1979.
22. **Efficacy of topical aciclovir for the treatment of feline herpetic keratitis: Results of a prospective clinical trial and data from in vitro investigations.** Williams DL, Robinson JC, Lay E, Field H. *Vet Rec* 157(9):254-257, 2005.
23. **Pharmacokinetics of acyclovir in the cat.** Owens JG, Nasisse MP, Tadepalli SM, Dorman DC. *J Vet Pharmacol Ther* 19(6):488-490, 1996.
24. **Effects of valacyclovir in cats infected with feline herpesvirus 1.** Nasisse MP, Dorman DC, Jamison KC, et al. *Am J Vet Res* 58(10):1141-1144, 1997.
25. **Substrate specificity and molecular modelling of the feline herpesvirus-1 thymidine kinase.** Hussein IT, Miguel RN, Tiley LS, Field HJ. *Arch Virol* 153(3):495-505, 2008.

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3. ***Plumb's Veterinary Drug Handbook***, 7th ed. Plumb DC (ed)–Ames: Wiley–Blackwell, 2011.
4. **Enrofloxacin-theophylline interaction: Influence of enrofloxacin on theophylline steady-state pharmacokinetics in the beagle dog.** Intorre L, Mengozzi G, Maccheroni M, et al. *J Vet Pharmacol Ther* 18(5):352-356, 1995.
5. **Ciprofloxacin-induced theophylline toxicity: A population-based study.** Antoniou T, Gomes T, Mamdani MM, Juurlink DN. *Eur J Clin Pharmacol* 67(5):521-526, 2011.
6. **Use of inhaled medications to treat respiratory diseases in dogs and cats.** Padrid P. *JAAHA* 42(2):165-169, 2006.
7. **Feline asthma: What's new and where might clinical practice be heading?** Venema CM, Patterson CC. *J Feline Med Surg* 12(9):681-692, 2010.
8. **Management of cardiac emergencies in small animals.** DeFrancesco TC. *Vet Clin North Am Small Anim Pract* 43(4):817-842, 2013.
9. **Hemodynamic effects of methylprednisolone acetate administration in cats.** Ployngam T, Tobias AH, Smith SA, et al. *Am J Vet Res* 67(4):583-587, 2006.
10. **Maintaining fluid and electrolyte balance in heart failure.** DeFrancesco TC. *Vet Clin North Am Small Anim Pract* 38(3):727-745, 2008.
11. **Feline diabetes mellitus: Diagnosis, treatment, and monitoring.** Rios L, Ward C. *Compend Contin Educ Pract Vet* 30(12):626-639, 2008.
12. **Feline diabetes mellitus: Clinical use of long-acting glargine and detemir.** Bloom CA, Rand J. *J Feline Med Surg* 16(3):205-215, 2014.
13. **Safety, pharmacokinetics and use of the novel NK-1 receptor antagonist maropitant (Cerenia) for the prevention of emesis and motion sickness in cats.** Hickman MA, Cox SR, Mahabir S, et al. *J Vet Pharmacol Ther* 31(3):220-229, 2008.
14. **Management of respiratory emergencies in small animals.** Sumner C, Rozanski E. *Vet Clin North Am Small Anim Pract* 43(4):799-815, 2013.
15. **Use of pimobendan in 170 cats (2006-2010).** Macgregor JM, Rush JE, Laste NJ, et al. *J Vet Cardiol* 13(4):251-260, 2011.
16. **Effect of oral administration of pimobendan in cats with heart failure.** Gordon SG, Saunders AB, Roland RM, et al. *JAVMA* 241(1):89-94, 2012.