Treatment of Feline Chronic Gingivostomatitis with Autologous Dendritic Cells from Blood Monocytes

Barbara Möhnle[a], Dierk E. Rebeski[b] and Thomas Grammel[b]
[a]Fachtierärztliches Zentrum für Kleintiere, Kehl, Germany, [b]PetBioCell GmbH, Osterode am Harz, Germany

Background & Objective

Feline chronic gingivostomatitis (FCGS) is a chronic disease of the oral mucosa that affects up to 26% of domestic cats. It is characterized by the formation of extensive inflammatory lesions in the oral cavity, including the area lateral to the palatoglossal folds. Clinical symptoms may be proliferative or ulcerative in nature, or even both. They are accompanied by moderate to severe pain in the mouth, loss of appetite, poor grooming, and reduced or absent socialization. Environment, diet, and housing conditions, dysbiosis of the oral microbiome, bacterial (*Fusobacterium nucleatum*, *Porphyromonas* and *Bartonella* species, *P. multocida* subsp. *multocida*) and viral infections such as feline calicivirus (FCV), feline herpesvirus type 1 (FHV-1), feline immunodeficiency virus (FIV), feline leukemia virus (FeLV), and the cat's compromised immune status contribute to the predisposition, onset, and persistence of the disease. Due to the unknown etiology - it appears to be an immune-mediated disease associated with chronic viral infections, particularly FCV - and the inadequate response to various treatment methods, cats are frequently euthanized.[1, 2] Reflecting the focus on immunomodulatory therapy, the study presents the results for 12 cats with severe clinical symptoms of FCGS who were treated postoperatively with autologous tolerogenic dendritic cells (tDCs) and followed up for up to 60 weeks.

[1]Soltero-Rivera, M., Goldschmidt, S., Arzi, B. 2023. Feline chronic gingivostomatitis current concepts in clinical management. J. Feline Med. Surg., 25 (8), 1-16. doi:101177/1098612X231186834. [2]Sánchez-Vallejo, M., Vélez-Velásquez, P., Correa-Valencia, M. 2025. Feline chronic gingivostomatitis: a thorough systematic review of associated factors. J. Feline Med. Surg., 27 (4), 1-8. doi:101177/1098612X241310590

Study Protocol

Study Protocol

- Period 12/10/2019 ongoing, each cat over 60 weeks
- Breed: 10 European Shorthair, 2 Siamese, kept partly in groups
- Sex and age: seven female, five male, all neutered, aged 1 - 14 years
- Clinical status: FHV-1 and FCV positive, FIV negative, FeLV negative, Mycoplasma negative
- Dental care prior to study: radiographic evaluation, tooth extraction for tooth resorption and root remnants, no dental treatment during the studying period
- Complete blood count, organ function tests (kidneys!)
- SDAI scoring
- Treatment: no corticosteroids, cyclosporine, interferon, or immunosuppressive medications, permission of pain relievers (NSAIDs), lactoferrin, L-lysine, antibiotics

Stomatitis Disease Activity Index (SDAI)

- Total score = 30
- Assessed by the owner and veterinarian
- Improvement: 0 = significant, 1 = slight, 2 = not, 3 = deterioration
- Weight: 0 = gain > 0.5 kg, 1 = gain > 0.25 kg, 2 = < 0.25 kg gain, 3 = loss
- Inflammation: 0 = none, 1 = mild, 2 = moderate, 3 = severe

Tab. 1. Stomatitis Disease Activity Index (SDAI).

Stomatitis Disease Activity Index (SDAI)		0	1	2	3
1	Owner's evaluation appetite/activity/grooming				
2	Owner evaluation comfort				
3	Maxillary buccal mucosal inflammation				
4	Mandibular buccal mucosal inflammation				
5	Maxillary attached gingival inflammation				
6	Mandibular attached gingival inflammation				
7	Molar salivary gland inflammation				
8	Inflammation of areas lateral to palatoglossal folds				
9	Oropharyngeal inflammation				
10	Lingual and/or sublingual inflammation				

Autologous Tolerogenic Dendritic Cells

Tolerogenic Dendritic Cells

- Derived from peripheral blood monocytes of the feline patient.
- ≥ 4 x 10^6 cells required for *in-vitro* culture in RPMI 1640, rf GM-CSF and rf IL-4 (day 1 to 6), rf IL-10 (day 5 and 6)
- Adherence to GMP compliance

Acceptance Criteria for Release

- Cell methods and FACS analysis
- Dose ≥ 1.5 x 10^5 / 2,0 ml of isotonic sodium chloride solution (0.9 %), cell viability ≥ 90 %, phenotype ≥ 10 % of MHC-II positive cells, sterility

Administration

- One dose (2 ml) intradermal injection within 24 h upon release

Course of the Disease

Observation Period (CW 0 to CW 60)

- Further monitoring of one cat (cont'd).
- Three cats not fully checked (n.a.).

Tab. 2. Overall SADI scores upon treatment (day 0).

	CW 0	CW 3	CW 12	CW 24	CW 36	CW 48	CW 60
Lilith	27	14	21	14	9	14	12
Azizi	24	4	0	n.a.	0	1	n.a.
Pablo	26	13	4	9	4	6	4
Beccy	20	15	16	14	11	24	12
Jack	27	21	16	13	n.a.	n.a.	n.a.
Sam	26	7	8	1	4	14	13
Nela	27	12	12	22	2	0	0
Bebe	18	15	6	4	n.a.	n.a.	n.a.
Leo	26	10	3	5	6	12	8
Bruno	27	24	12	8	8	0	0
Birdy	24	18	9	7	0	0	0
Dajo	24	14	8	cont'd	cont'd	cont'd	cont'd
Lowest value	18	4	0	1	0	0	0
Highest Value	27	24	21	22	11	24	13
Median	26	14	8,5	8,5	4	6	6
95% CI for the median	24,00-27,00	10,35-17,48	4,35-15,31	4,48-14,00	0,28-8,86	0,00-14,00	0,00-12,19

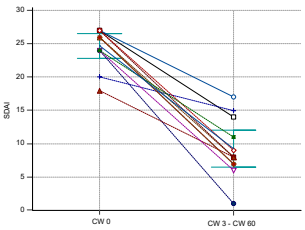

Fig 1. Significant difference, p = 0,0001, in SDAI scores before (CW 0) and after treatment (CW 3 - CW 60), n= 12, paired t-test[3].

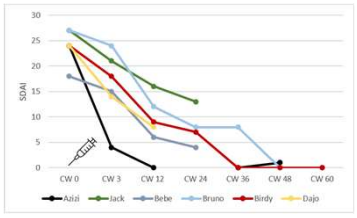

Fig. 2. Group 1 consists of cats whose SDAI scores steadily decreased upon treatment, p = 0,0269, n = 6, paired Wilcoxon test.[3]

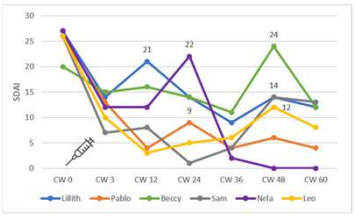

Fig. 3. Group 2 comprises cats whose SDAI-scores showed unexpected "peaks" upon treatment, p = 0,0260, n = 6, paired Wilcoxon test.[3]

[3]MedCalc Statistical Software Version 23.5.5 (MedCalc Software Ltd, Ostend, Belgium; https://www.medcalc.org; 2026)

Discussion & Conclusion

- Twelve cats with severe FCGS (median SDAI score of 26, 95% confidence interval for the median ranging from 24 to 27) were admitted to a veterinary hospital. Following a standardized protocol, the cats were treated with a single intradermal injection of tDCs derived from autologous blood monocytes. On day 0 (treatment), the SDAI scores were recorded and then monitored at calendar weeks 3, 12, 24, 36, 48, and 60.

- All cats tolerated the tDC-based immunotherapy well, with no side effects attributable to the cell suspension. Overall, the SDAI scores decreased to varying degrees in all cats three weeks after the intradermal injection, with one cat scoring a value of 0. Statistical analysis of the clinical course in all cats (n = 12) revealed a significant difference in SDAI scores before and after treatment (paired t-test, p < 0.0001). Interestingly, although the clinical course tended toward remission, the values varied both within and between cats; in some the values decreased consistently (group 1, n = 6, Fig. 1), suggesting continuous improvement, while in others unexpected "peaks" occurred at various time points (group 2, n = 6, Fig. 2). For both groups, the results showed a significant difference (p = 0.0269, p = 0.0260) before and after treatment, regardless of the trend in the scores. Particularly in cats in group 2, additional administration of tDCs at the time when scores rise could be considered appropriate to re-modulate the immune response to refractory FCGS.

- There are various reports on immunomodulatory action based on cells other than tDCs namely autologous or allogenic fresh adipose-derived mesenchymal stem cells (MSCs).[4, 5, 6, 7]. An assessment of certain aspects of the preparation, legal framework, and logistical arrangements, as summarized in Table 3, would support the use of tDCs.

Tab. 3 Aspects of the use of MSCs versus tDCs.

	Adipose-derived mesenchymal stem cells (MSCs)	Monocyte-derived tolerogenic dendritic cells (tDCs)
Surgery	Yes (or donor)	No
Autologous	No (yes)	Yes
Cell origin	Fat tissue	Blood monocytes
Preparation	24 hours plus shipping	6 days plus shipping
Sterility	Risky (after 24 h)	1/137 (0,73%) 2025
GMP	?	Established
Cryopreservation	Yes	No (not recommended)
Time to treatment	Short	Extended
Administration	Intravenous	Intradermal

- To conclude: At a veterinary clinic, tDC-based immunotherapy successfully improved the clinical course of FCGS. We are seeking further studies and collaborative partners to further validate our preliminary results.

[4]Arzi, B., Mills-Ko, E., Verstraete, F.J., et al. 2016. Therapeutic efficacy of fresh, autologous mesenchymal stem cells for severe refractory gingivostomatitis in cats. Stem Cells Transl Med, 5, 75-86. [5]Arzi, B., Peralta, S., Fiani, N. et al. 2020. A multicenter experience using adipose-derived mesenchymal stem cell therapy for cats with chronic, non-responsive gingivostomatitis. Stem Cell Res Ther, 11, 115. doi: 10.1186/s13287-020-01623-9. [6]Arzi, B., Clark, K.C., Sundaram, A., et al. 2017. Therapeutic efficacy of fresh, allogenic mesenchymal stem cells for severe refractory feline chronic gingivostomatitis. Stem Cells Transl Med, 6, 1710-1722. [7]Rivas, I.L., Soltero-Rivera, M., Vapniarsky, N. et al. 2023. Stroma cell therapy in cats with feline chronic gingivostomatitis: current perspectives and future direction. J Feline Med Surg, 25. doi: 10.1177/1098612X23185395.