Combined MSC-antiviral treatment for systemic inflammation and lymphoid tissue regeneration in cats with FIP

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STAR 2023
Feline Infectious Peritonitis (FIP)

- Occurs mostly in cats <16 months
- Highly fatal if untreated
- Caused by feline enteric coronavirus (FECV)

Drechsler et al., 2011
Pedersen, 2014

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FIP Clinical Disease

• Multi-system inflammation
• Pyogranulomas
• Lymphopenia
• Effusive (“wet”) and non-effusive (“dry”) forms
Multipotent Stromal Cells (MSCs)

Bone marrow  Adipose tissue  Muscle  Neonatal tissues  Dental pulp  Skin

Multipotent stromal cell (MSC)

immunomodulation

Singer & Caplan, 2011
Multipotent Stromal Cells (MSCs)

- Successfully treated refractory chronic oral inflammatory disease in cats
- Use in other viral inflammatory disease
  - Increased survival, reduced levels of pro-inflammatory cytokines, and increased lung tissue regeneration in patients with severe COVID-19 infection and pneumonia

Arzi et al., 2017
Shi et al. 2021
Natasha Holden 2022
**GS-441524**

- Nucleoside analog
- Effective in ~80% of FIP cases
  - Some cats relapse post-treatment


Murphy et al., 2018
Rationale

• Poor understanding of immune recovery with GS-441524 alone

• MSC potential to:
  • improve immune recovery
  • shorten treatment duration
Hypothesis

• Addition of MSCs to GS-441524 antiviral treatment for FIP will decrease systemic inflammation and facilitate lymphoid recovery

Expectations:

↓ Pro-inflammatory cytokines

↑ Lymphocyte counts
Clinical Trial Study Design

- **Week 0**: Start GS-441524
- **Week 1**: MSCs/saline
- **Week 3**: MSCs/saline
- **Week 5**: MSCs/saline
- **Week 7**: MSCs/saline
- **Week 9**: MSCs/saline
- **Week 11**: MSCs/saline

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Cytokine Assay

- Combination of ELISA and flow cytometry techniques
- Millipore Multiplex Feline-Specific Cytokine Assay
Blood Smear Interpretation

• Manual 400-cell differential leukocyte counts
• Calculate cell populations using differential % x total leukocytes from CBC

Results: Cytokine Panel

Innate Immunity

IL-1β Concentration

Week 0 Week 7 Week 11

IL-6 Concentration

Week 0 Week 7 Week 11

IL-18 Concentration

Week 0 Week 7 Week 11

- MSC-GS
- GS only
- Control-SPF
Results: Cytokine Panel

T-Cell Polarization

- IFN\(\gamma\) Concentration
- IL-4 Concentration
- IL-12 Concentration

- MSC-GS
- GS only
- Control-SPF
Results: Cytokine Panel

- **IL-1β Concentration**
- **IL-6 Concentration**
- **IL-18 Concentration**
- **IFNγ Concentration**
- **IL-4 Concentration**
- **IL-12 Concentration**

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**Legend:**
- MSC-GS
- GS only
- Control-SPF
Results: Hematology Data

Lymphocyte Counts

- MSC-GS
- GS only
- Control-SPF
Results: Hematology Data

Segmented Neutrophil Counts

Band Counts

Eosinophil Counts

- MSC-GS
- GS only
- Control-SPF
Discussion

- No adverse effects of MSCs
  - No “immunosuppressive” effects
  - No thrombosis
Discussion

• Why didn’t we see a difference with the addition of MSCs?
  • Effusive FIP is effectively treated by GS-441524
  • Sample size too small
  • Naturally-occurring FIP – different stages of disease on presentation
  • Screening selected for less severely affected cats
Future Directions

• Correlation of cytokine patterns and hematologic results

• Use of MSCs with non-effusive FIP
  • Harder to treat with antiviral alone
Acknowledgements

• Kol Lab
  • Dr. Amir Kol
  • Dr. Patrawin Wanakumjorn
  • Dr. Diego Castillo
• Dr. Brian Murphy
• Dr. Krystle Reagan & the VCCT Team

Participating clients and cats!

Financial support provided by UC Davis STAR Program, National Institutes of Health, National Institute of Child Health and Development
References


