

## MSCs in fistulizing Crohn's disease - ADMIRE-CD

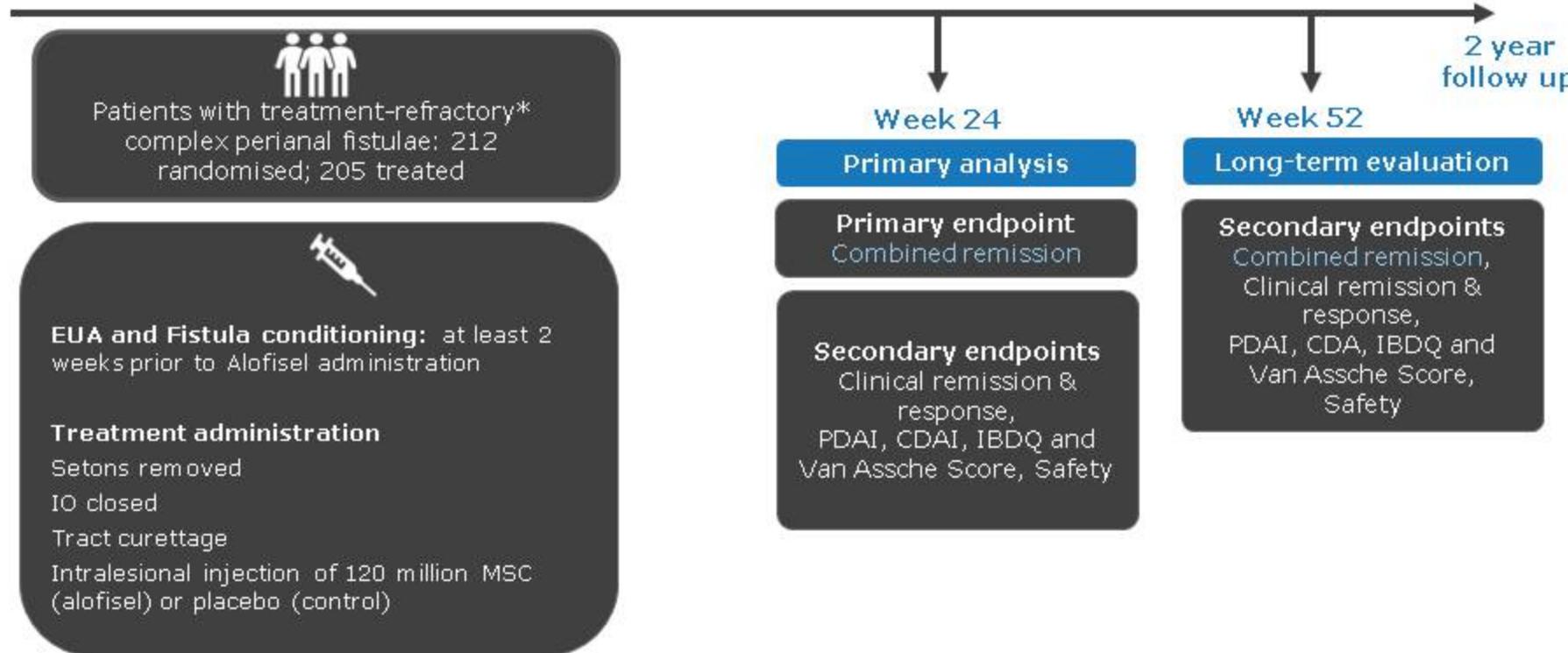
THE LANCET

Expanded allogeneic adipose-derived mesenchymal stem cells (Cx601) for complex perianal fistulas in Crohn's disease: a phase 3 randomised, double-blind controlled trial

Gastroenterology

**Long-term Efficacy and Safety of Stem Cell Therapy (Cx601) for Complex Perianal Fistulas in Patients With Crohn's Disease**

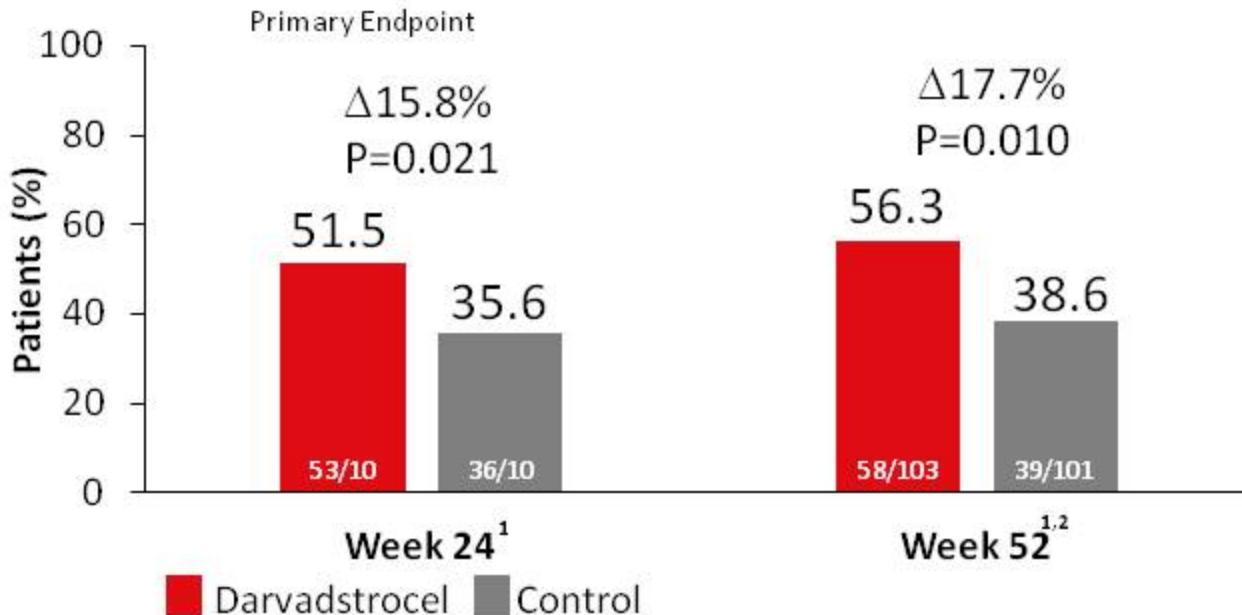
## ADMIRE-CD phase III clinical trial design<sup>1,2</sup>





## Combined remission\* at week 24 and week 52

mITT POPULATION (n=204)



<sup>1</sup>Panes *The Lancet* 2016;388:1281–90, <sup>2</sup>Panes *Gastroenterology* 2018;154:1334–42

# Cell therapy in IBD

**Nick Powell**

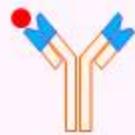
## Disclosures

I have received lecturing fees, consultancy fees and/or grants from:

AbbVie	Ferring
Allergan	Janssen
Bristol Myers-Squibb	Takeda
Celgene	Tillotts
Dr Falk Pharma UK Ltd	Vifor
Debiopharm	
Eli-Lilly	

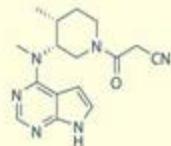
# Emerging treatment landscape in IBD

## mAb



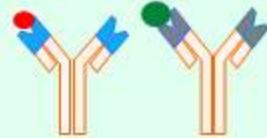
- Anti-integrin β7
- Anti-MAdCAM1
- Anti-IL23p19
- Anti-IL6
- Anti-NKG2D
- Anti-IL21

## Small molecule inhibitors



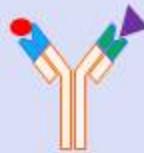
- JAK inhibitors
- Apremilast
- Ozanimod

## Novel combinations



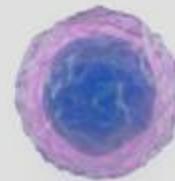
- Anti-TNF
- Anti-IL23p19

## Bispecific Abs



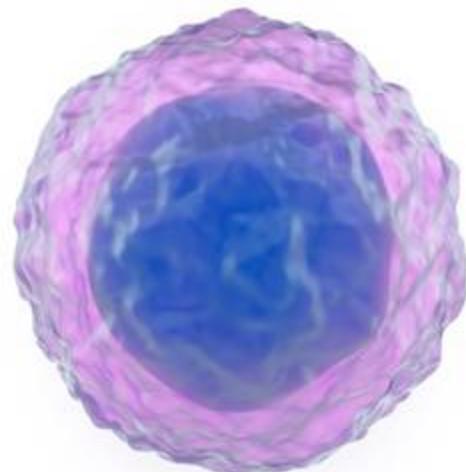
- Anti-TNF/IL17A

## Cell therapy



## Cell therapy

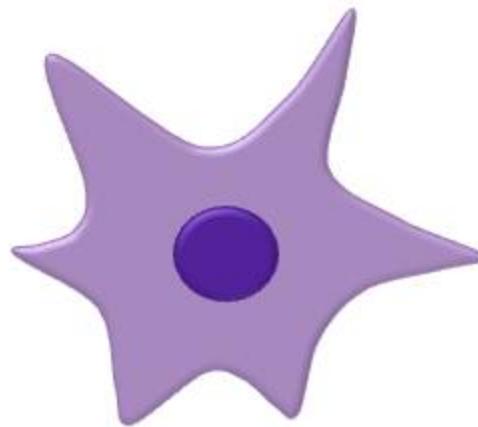
-  Polyfunctional
-  Reactive & adaptable
-  Plausible Biological function
-  Editable function
-  Personalized possibility



## Cell therapy options for IBD



Haemopoietic Stem Cells

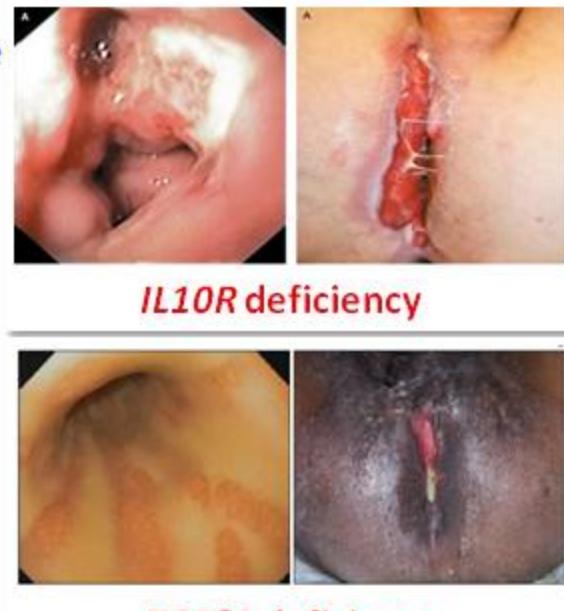
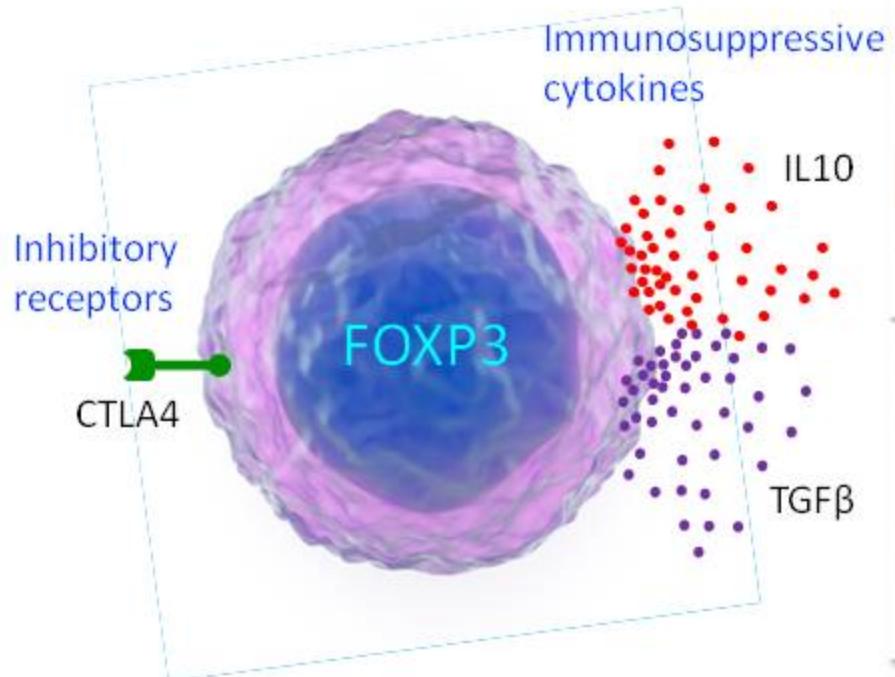
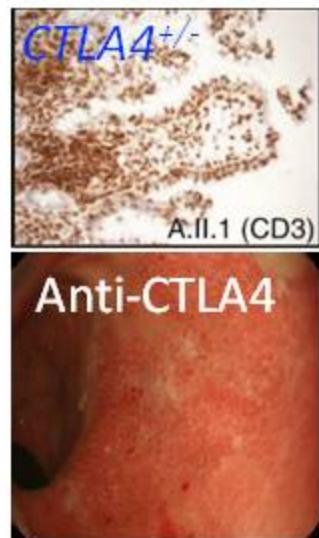


Mesenchymal stem cell



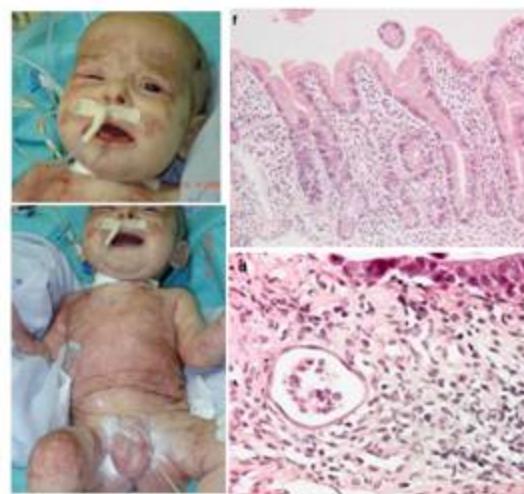
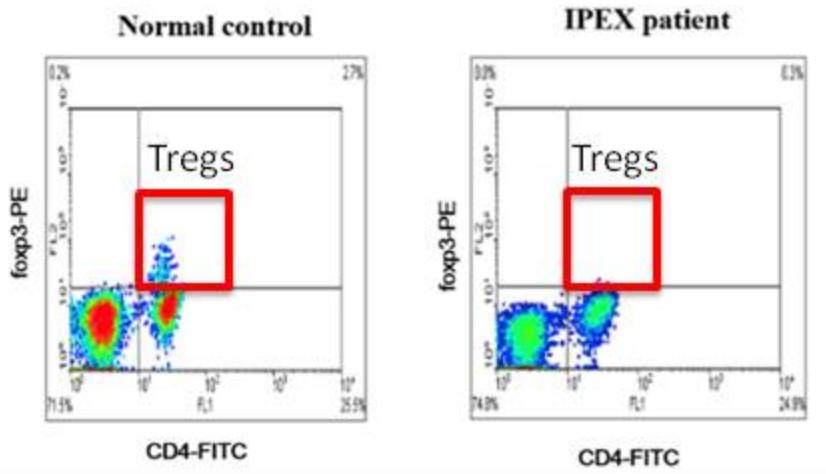
Regulatory T-cell

## Regulatory T-cells

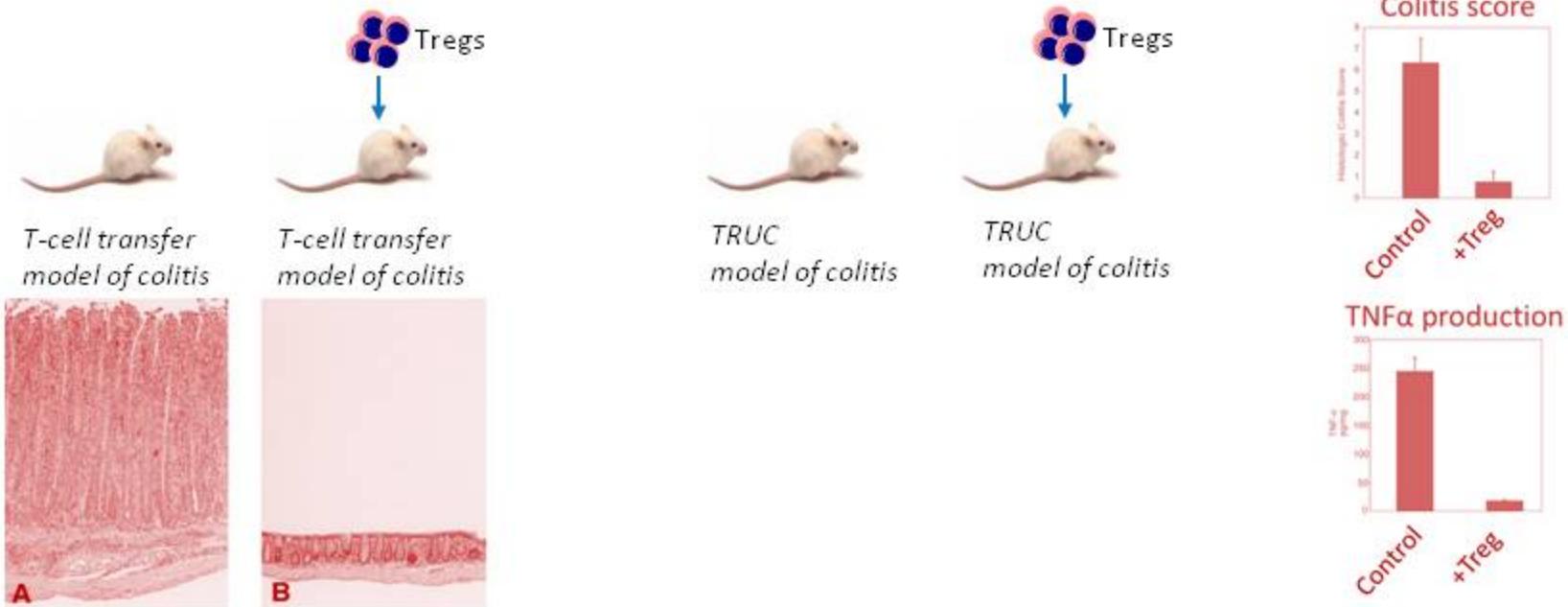


# Regulatory T-cells are essential for maintenance of intestinal homeostasis

Immune dysregulation polyendocrinopathy enteropathy X-linked syndrome



## Tregs control experimental colitis



# The TRIBUTE study

Isolate PBMCs



Purify Tregs



Expand



Clinical grade reagent



# Mesenchymal Stem Cells (MSC)

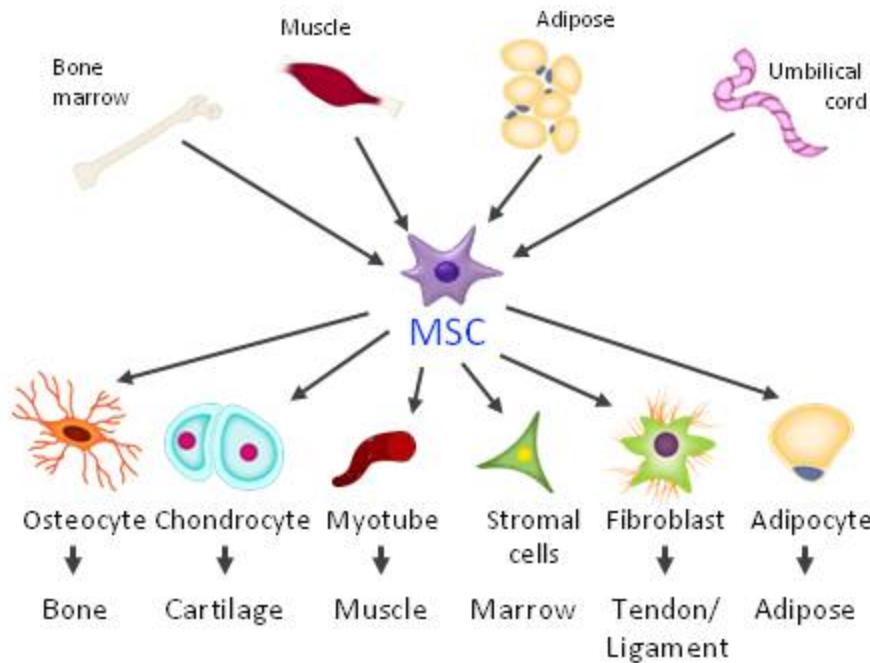
Fibroblast-like cells that can be isolated from different tissue sites

Able to differentiate into a different stromal cell lineages

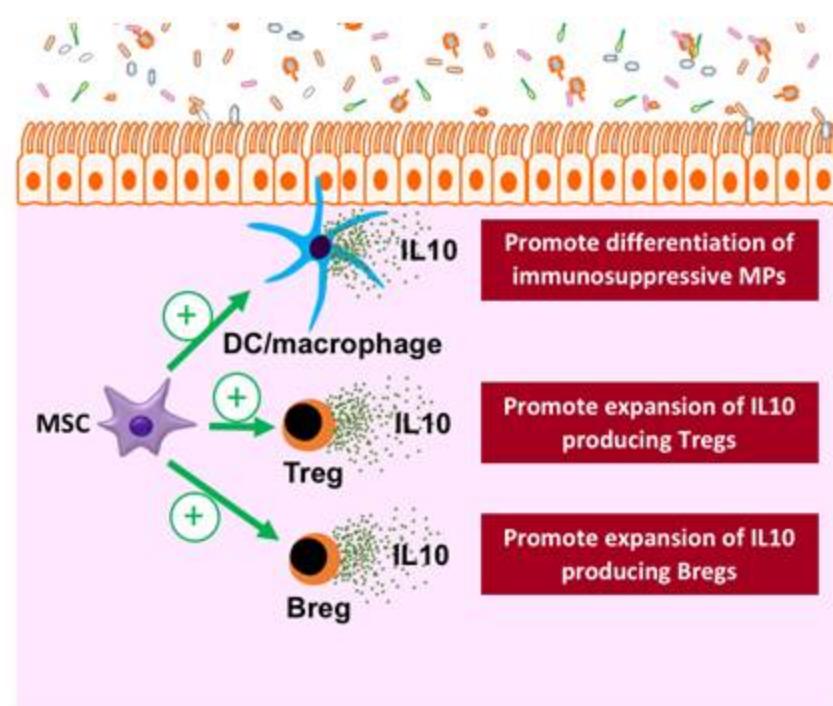
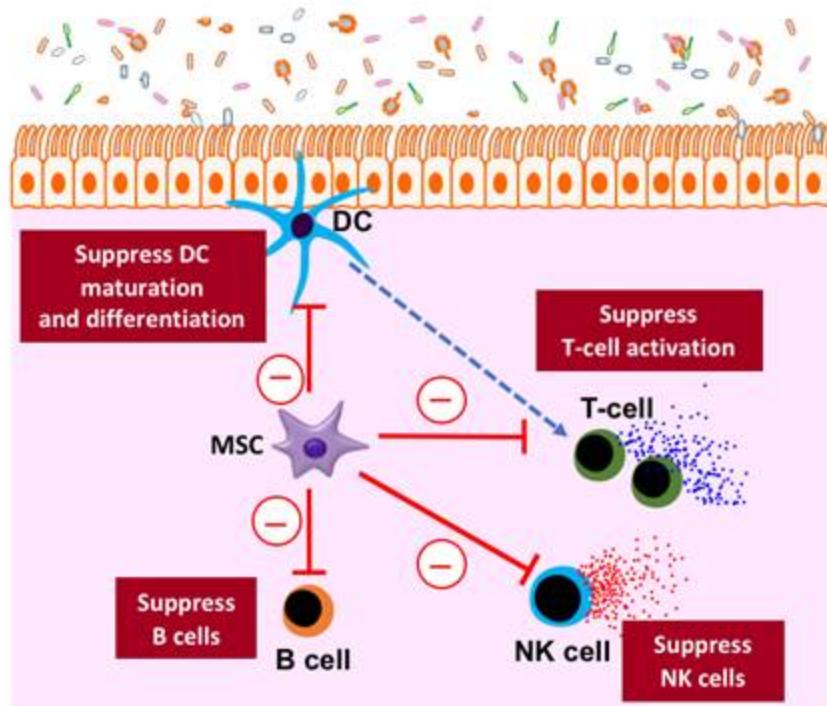
Can be readily expanded *in-vitro*

Anti-inflammatory activity

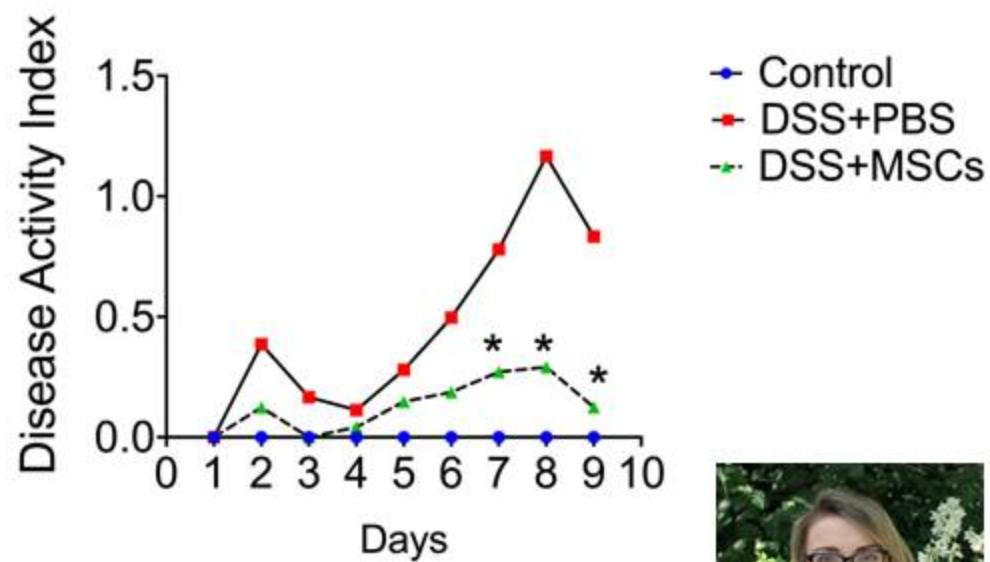
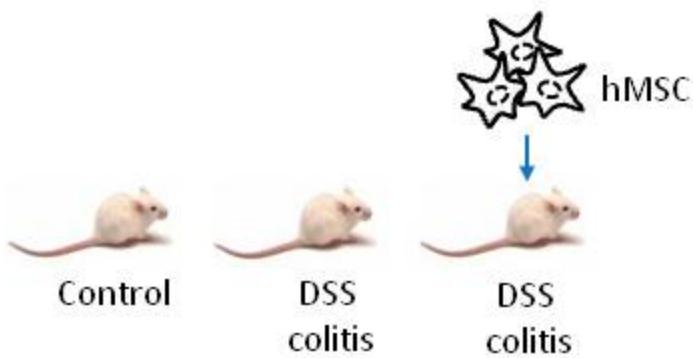
Tissue repair properties



## Anti-inflammatory activity of MSCs



## MSC suppress preclinical models of colitis



# Autologous adipose-derived MSC for complex perianal fistulas

Garcia-Olmo D, et al. 2009



Autologous adipose-derived MSCs



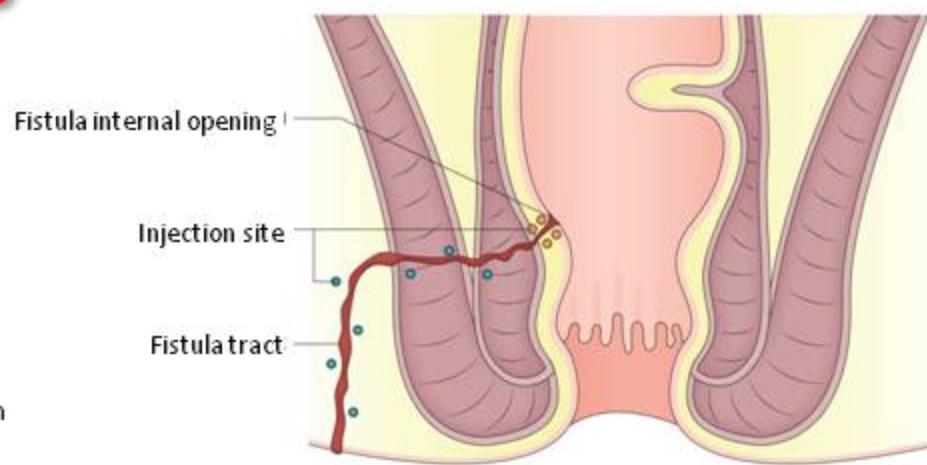
Randomized active-controlled open-label study



49 patients with complex perianal fistulas

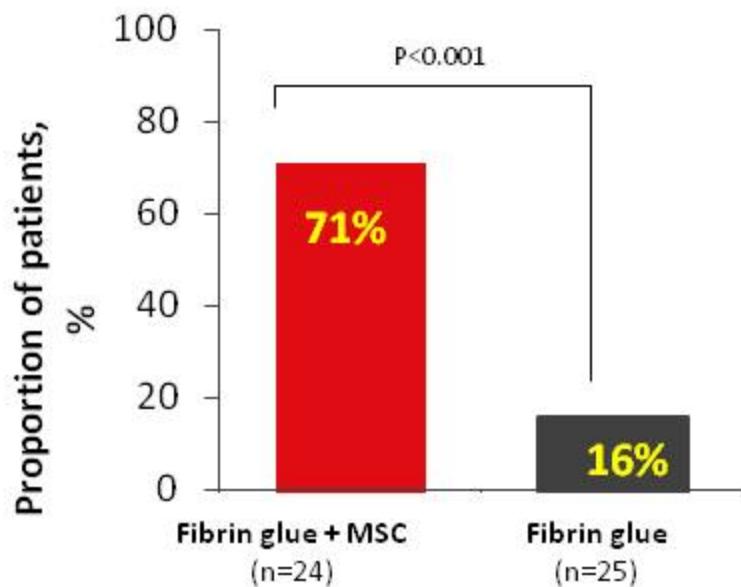


Intra-lesional injection of 20 million MSCs with fibrin glue, or fibrin glue alone. Both treatment arms had tract curettage and sealing, closure of internal opening



## Autologous adipose-derived MSC for complex perianal fistulas

Healing of complex fistula 8 weeks after last treatment



## MSCs in fistulizing Crohn's disease - ADMIRE-CD

THE LANCET

### Phase 3, randomized, double blind, controlled study



Objective: to determine the efficacy/safety of a single injection of 120 million adipose-derived MSC (darvadstrocel) for complex perianal fistulas in CD

(Cx601) for Complex Perianal Fistulas in Patients  
With Crohn's Disease

## ADMIRE-CD phase III clinical trial design<sup>1,2</sup>



Patients with treatment-refractory\* complex perianal fistulae: 212 randomised; 205 treated



EUA and Fistula conditioning: at least 2 weeks prior to Alofisel administration

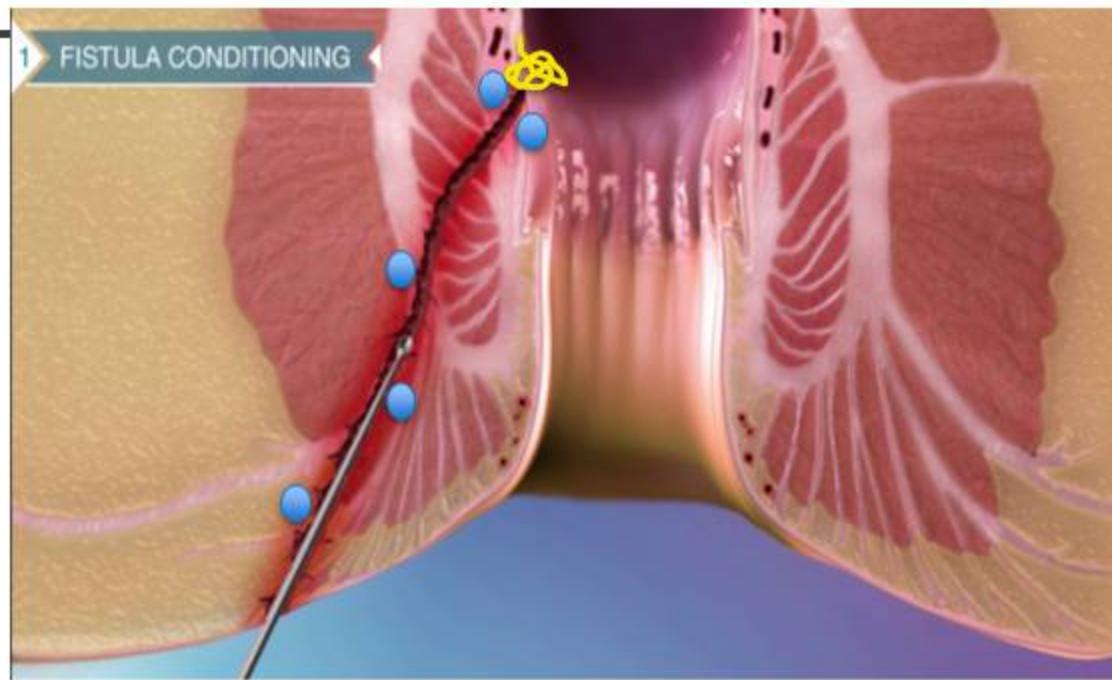
### Treatment administration

Setons removed

IO closed

Tract curettage

Intralesional injection of 120 million MSC (aloferisel) or placebo (control)

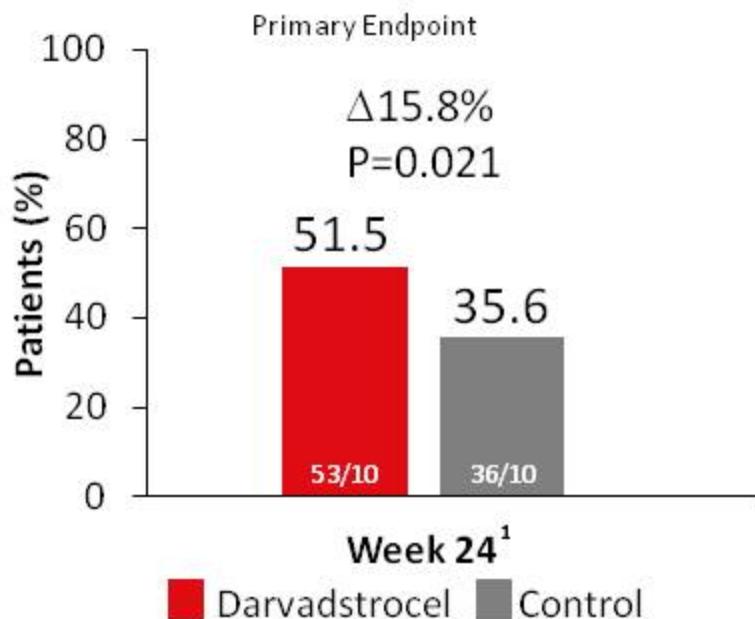


## Baseline patient and disease characteristics

Baseline characteristics	Alofisel (n=103)	Control (n=101)
Mean age, y (SD)	38.9 (13.1)	37.7 (13.1)
Men, N (%)	57 (55.3)	53 (52.5)
Mean CD duration, y (SD)	11.8 (9.8)	11.4 (9.0)
Mean PDAI score*, (SD)	6.7 (2.5)	6.5 (2.8)
Fistula external openings (%)		
1	58 (56.3)	72 (71.3)
2	37 (35.9)	25 (24.8)
>2	8 (7.8)	4 (4.0)
Mean CDAI score† (SD)	87.8 (48.3)	93.3 (55.0)



## Combined remission\* at week 24 and week 52 mITT POPULATION (n=204)



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## Summary



Cell therapies are emerging into clinical practice



MSCs are effective in complex perianal, fistulizing CD



Tregs are effective in preclinical IBD models and clinical trials are starting