

OSE IMMUNO
THERAPEUTICS



Anti-IL-7 receptor plus anti-IL12/23 combination induces complete histological normalization in chronic colitis

February 20th, 2025

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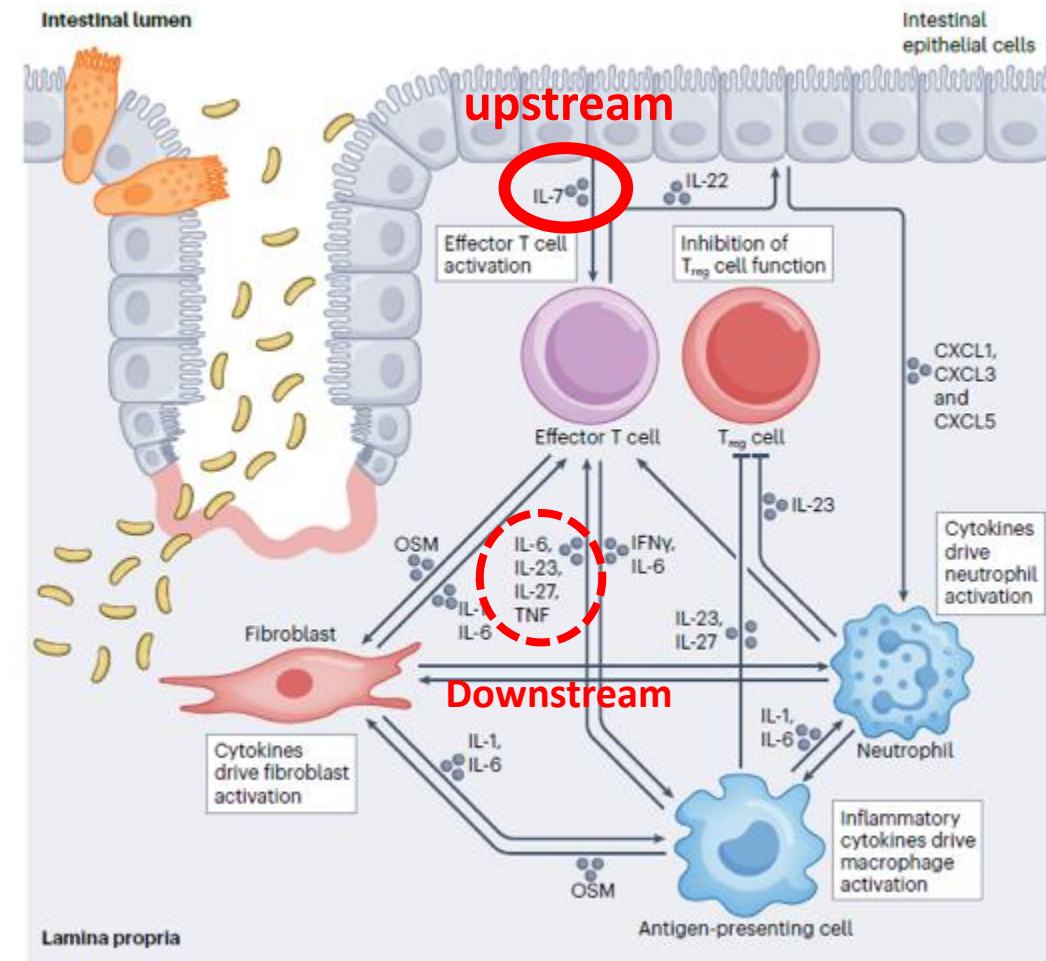
IL-7 fuels chronic inflammation in Tissues

Upstream mechanism of resistance in hyper-inflammation

The 'angry' cell concept and resistance to anti-cytokine therapies.

“Recent evidence suggests the presence of highly pro-inflammatory — or ‘angry’ — cells in the intestinal mucosa in inflammatory bowel disease (IBD) that drive molecular resistance to anti-cytokine therapy (such as anti-TNF and anti-IL-12/IL-23 therapies). »

« Intestinal epithelial cells (IECs) produce cytokines such as **IL-7** to activate effector T cells and can produce chemokines such as CXCL1, CXCL3 and CXCL5 to induce neutrophil recruitment and activation.”

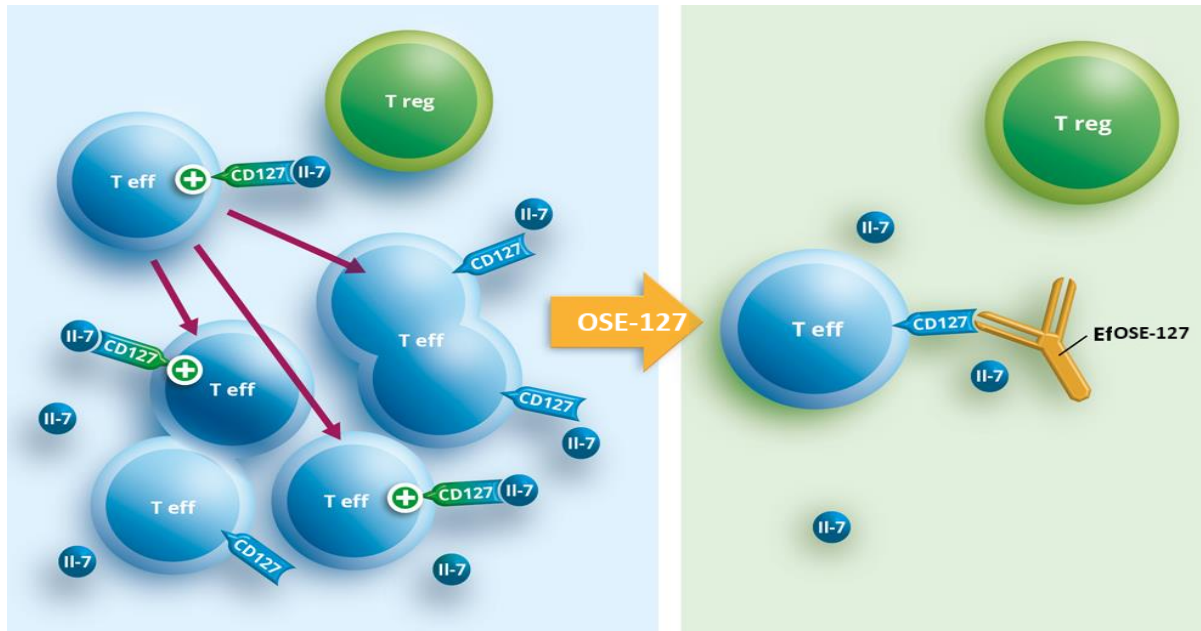


Neurath M. Nature Review Immunology 2024

Lusvertikimab / OSE-127

Pure IL-7 receptor antagonist mAb

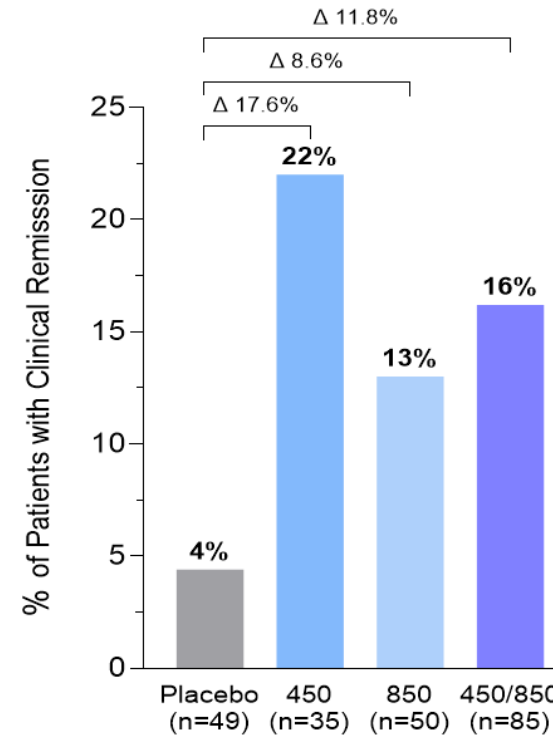
Tackling the fuel of memory T-lymphocytes while sparing Tregs



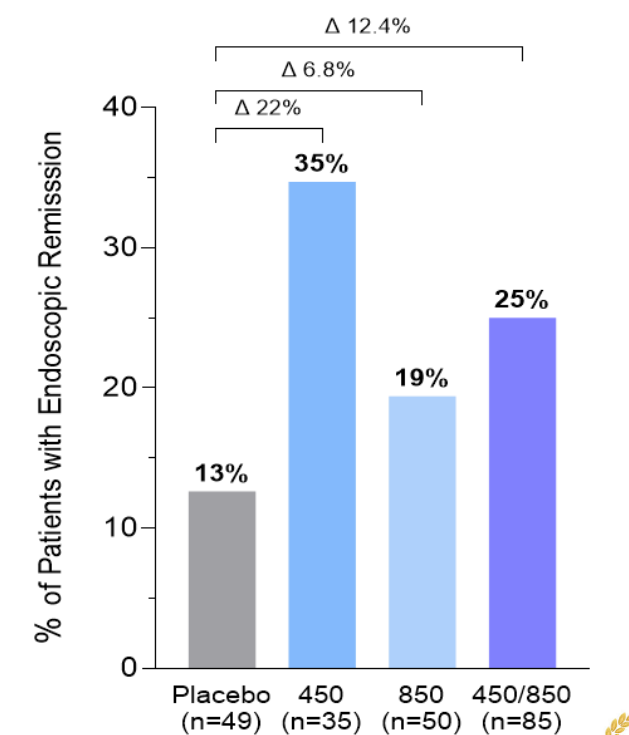
Positive Phase 2 results in Ulcerative Colitis

ECCO 2025: #OP-36

Clinical Remission (W10)



Endoscopic Remission (W10)



European
Crohn's and Colitis
Organisation



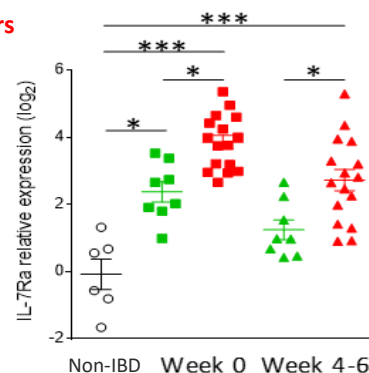
IL-7R over-expression in Bio-refractory IBD patients

High IL7R pathway expression in patient's refractory to anti-TNF, anti- $\alpha 4\beta 7$ or anti-IL12/23 therapies

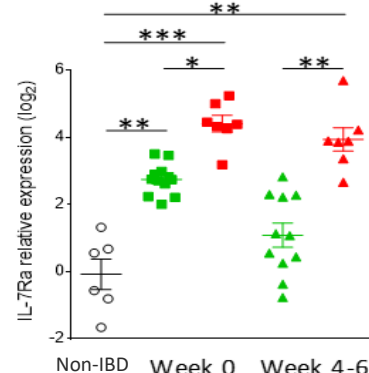
Mucosal IL7R pathway over-expression in IBD
Correlation with anti-TNF or Vedolizumab unresponsiveness

Ulcerative Colitis

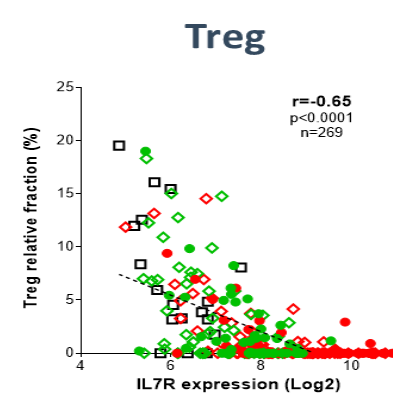
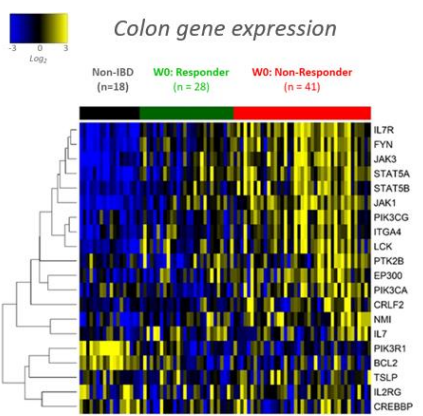
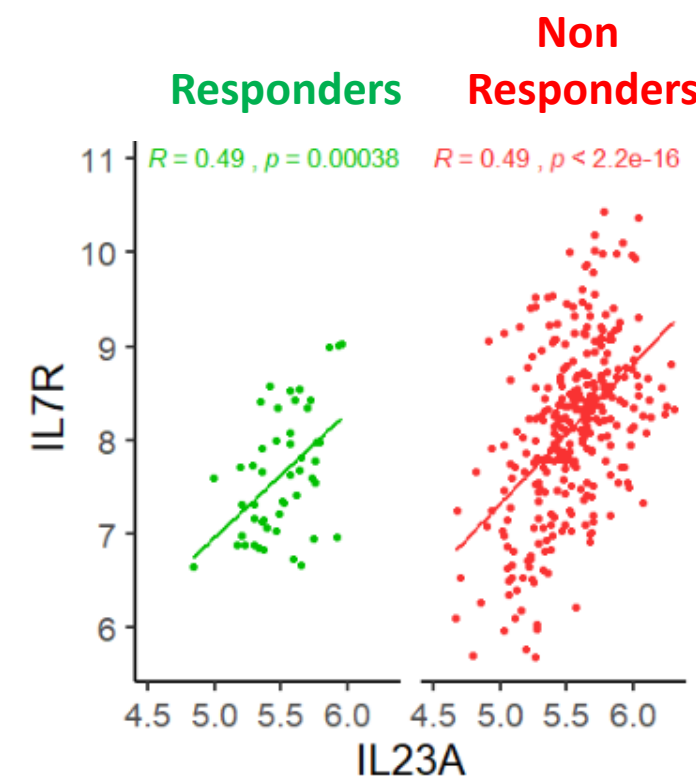
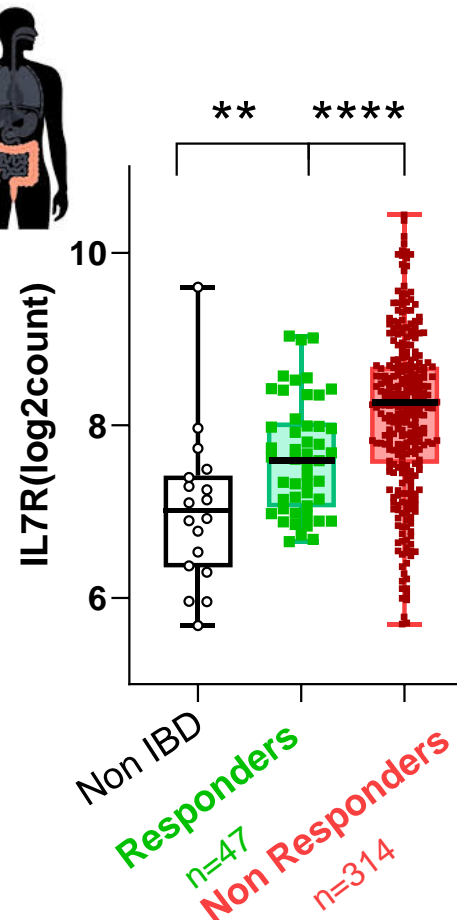
Responders
Non-responders



Crohn Disease



IL7R mucosal over-expression in Ustekinumab UC patients
High correlation between IL7 Receptor and IL23 cytokine expression

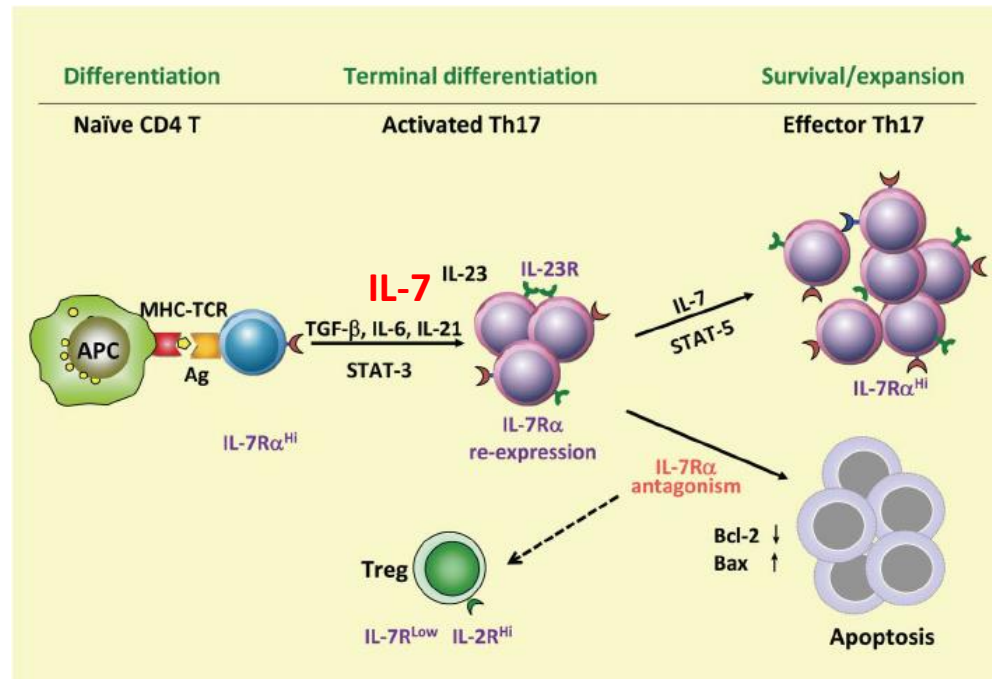
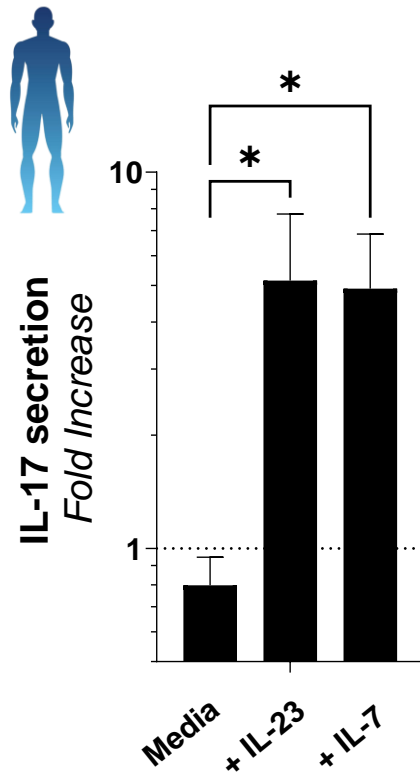


IL-7 impacts IL23-dependant human Th17 cell biology

IL23 antagonist loss of efficacy in presence of IL-7

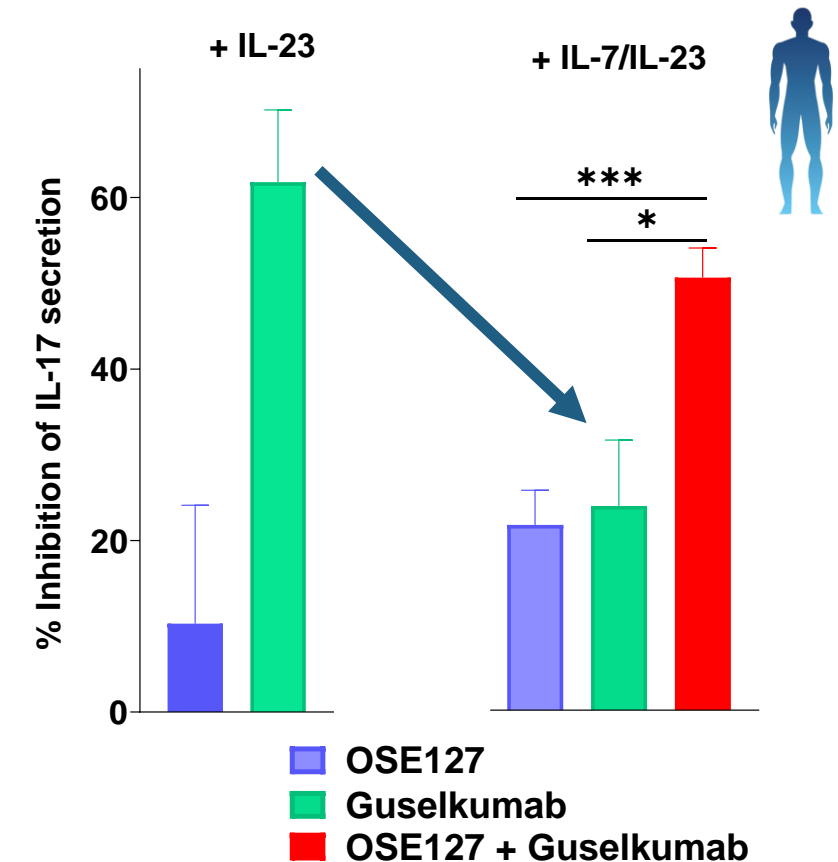
Model: naïve human primary T cells differentiation in IL17-secreting cells

IL-7 induces Th17 cells



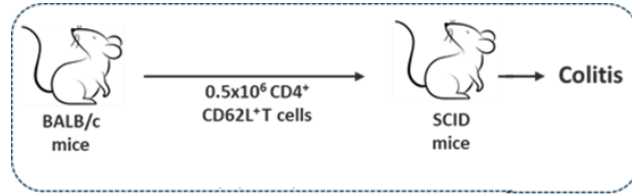
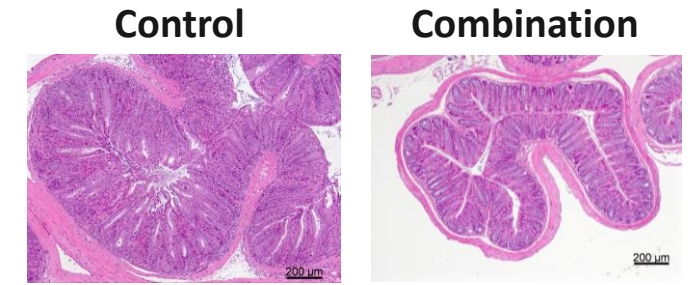
Leung et al. Cell & Mol Immunol 2010

IL-7 drives IL-23 antagonist resistance

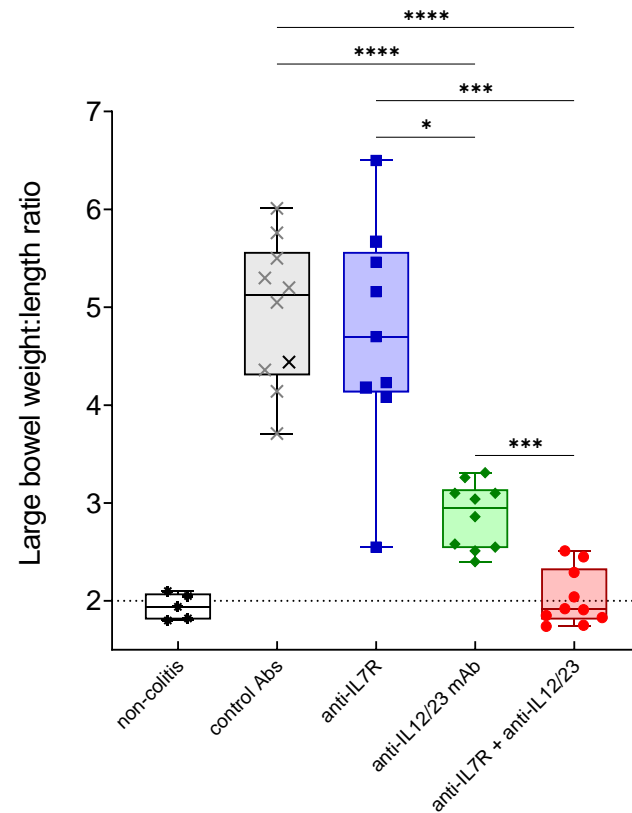


IL-7R + IL12/23 blockade induces mucosal healing

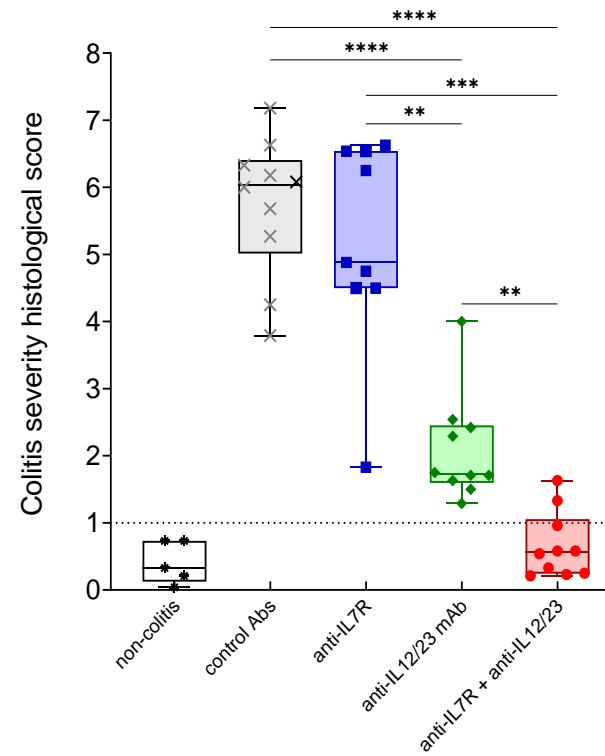
T-cell transfer colitis mouse model (refractory model to IL7R monotherapy)



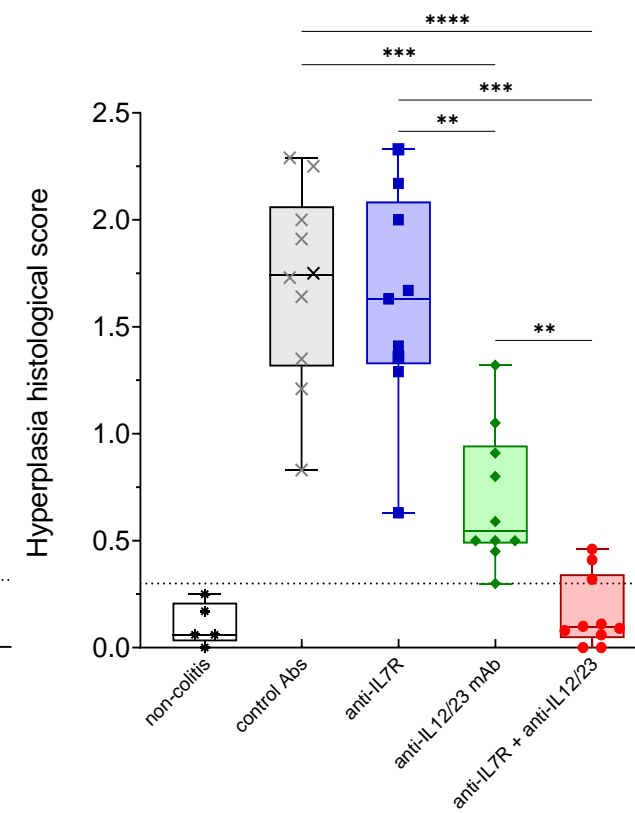
Colon weight:Length ratio



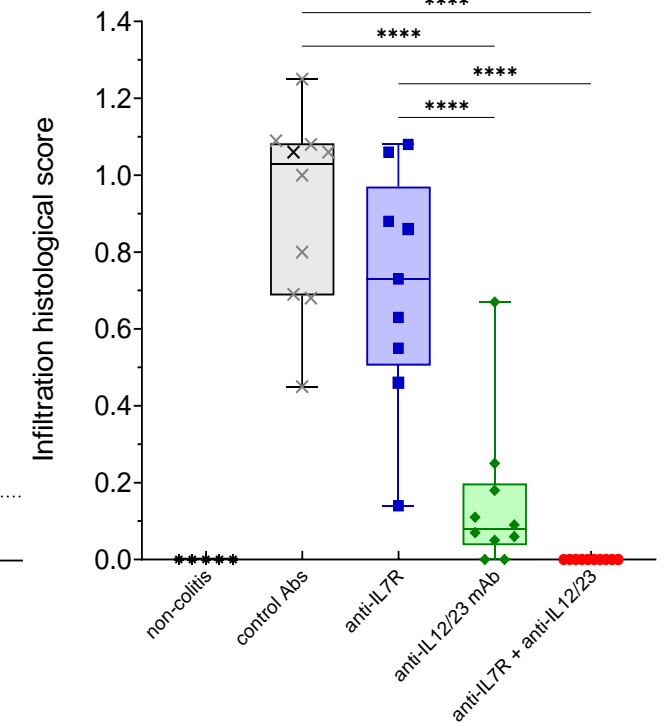
Histological lesions



Epithelial Hyperplasia

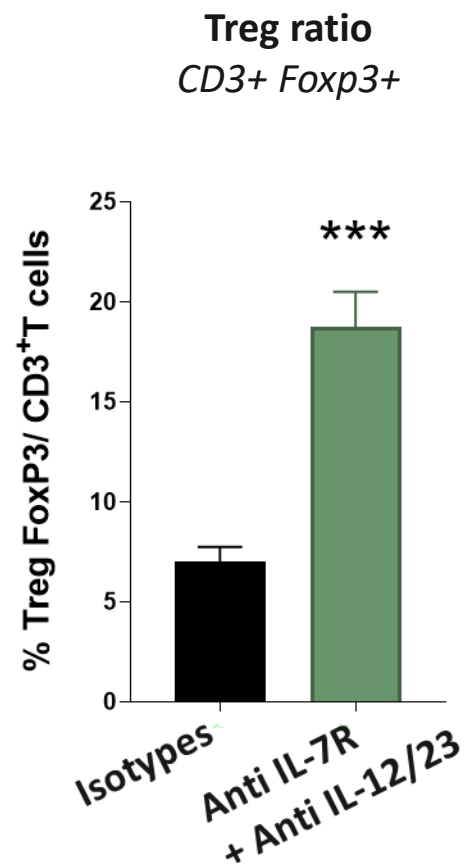
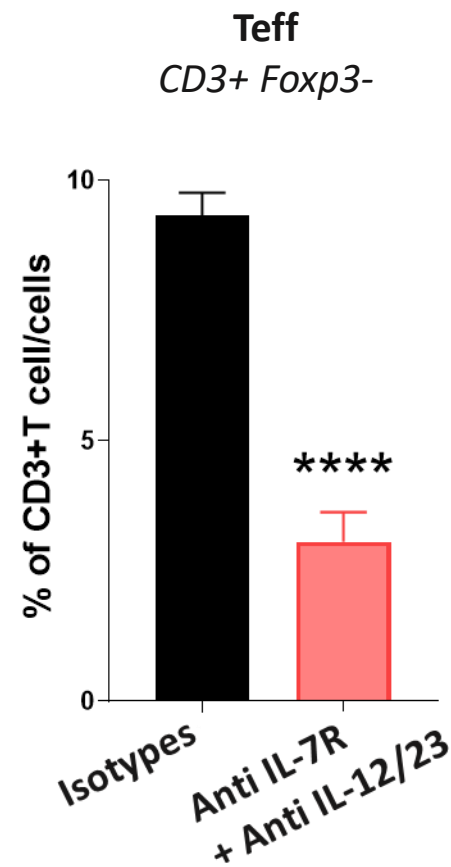


Immune Infiltrates

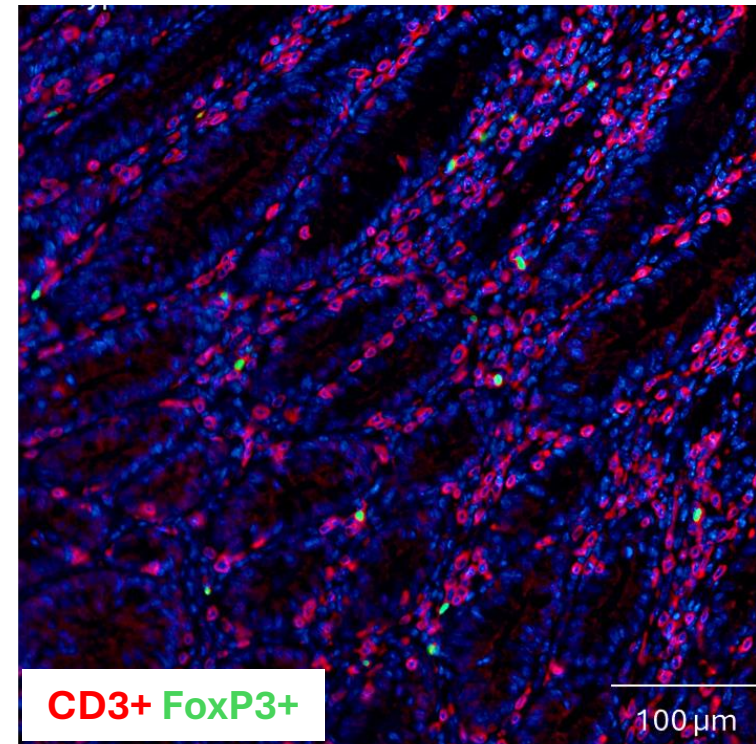


Anti-IL7R + anti-IL12/23 significantly modifies immune infiltrates

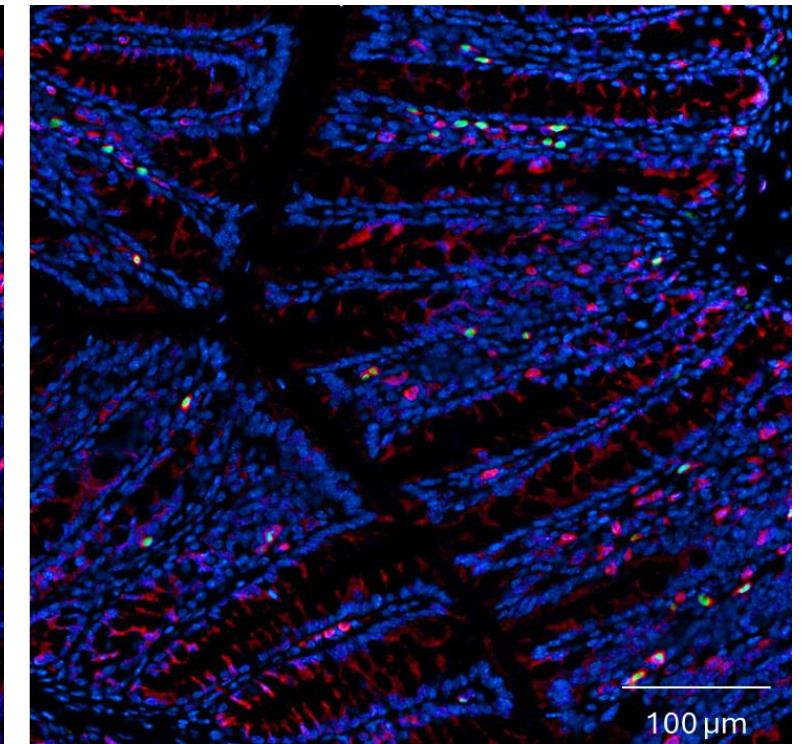
Increases mucosal Treg/Teff ratio



Control

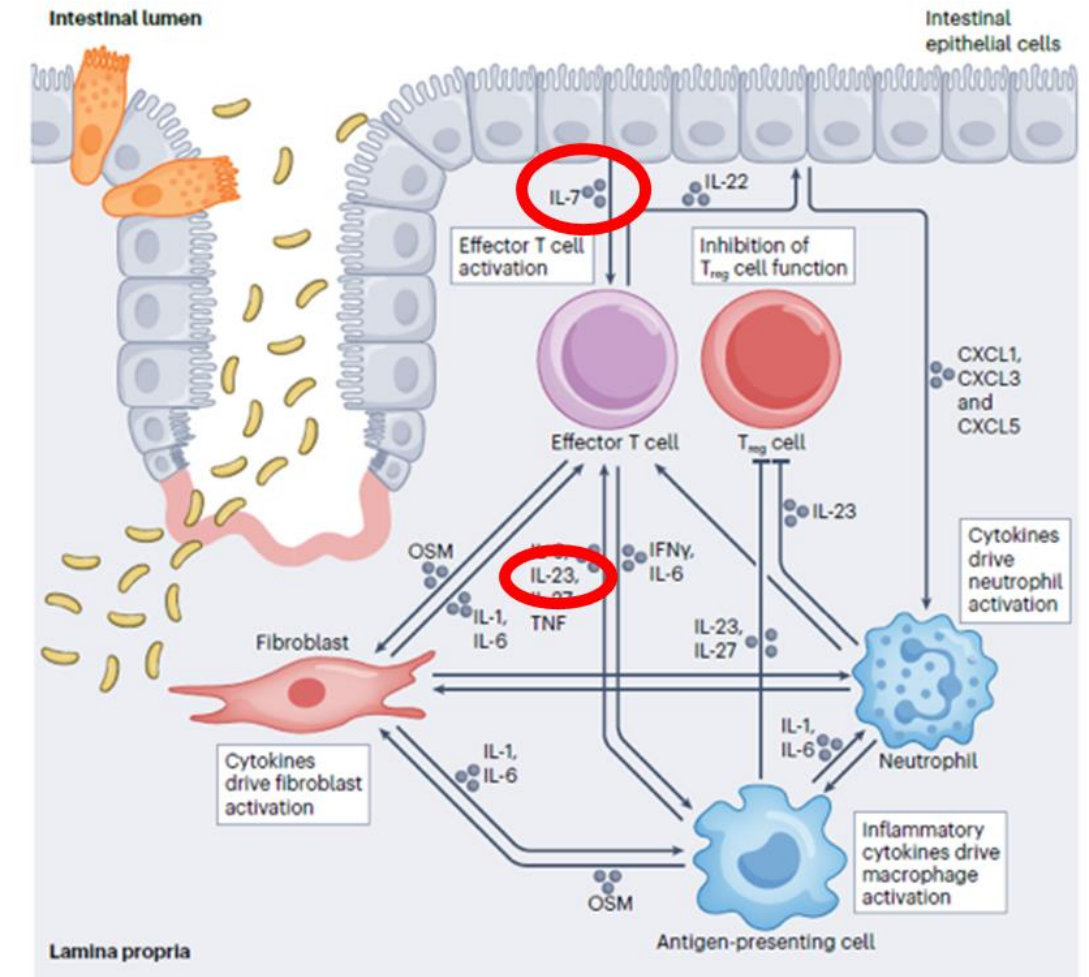


Combination



Summary

- ❑ **Anti-IL7R mAb (Lusvertikimab) monotherapy** induces **Clinical & Endoscopic Remission** in UC patients
- ❑ **IL7R mucosal over-expression** in anti-TNF / anti-Integrin / anti-IL12-23 refractory IBD patients
- ❑ **IL7 drives anti-IL23 resistance** (*human Th17 cell in-vitro model*)
- ❑ **Anti-IL7R (upstream) + anti-IL12/23 (downstream) combination** induces high preclinical efficacy and complete **mucosal normalization/healing** (*chronic colitis mouse model*)



Neurath M. Nature Review Immunology 2024

OSE IMMUNO THERAPEUTICS



Nicolas Poirier, CEO

nicolas.poirier@ose-immuno.com

Head Office

22, boulevard Bénoni Goullin
44200 Nantes, France

Paris Office

10, Place de Catalogne
75014 Paris, France

Company Information: <http://ose-immuno.com/en/>