The Future of IBD Therapy

Trusha Patel, MD

Assistant Professor of Pediatrics
Division of Gastroenterology, Hepatology and Nutrition



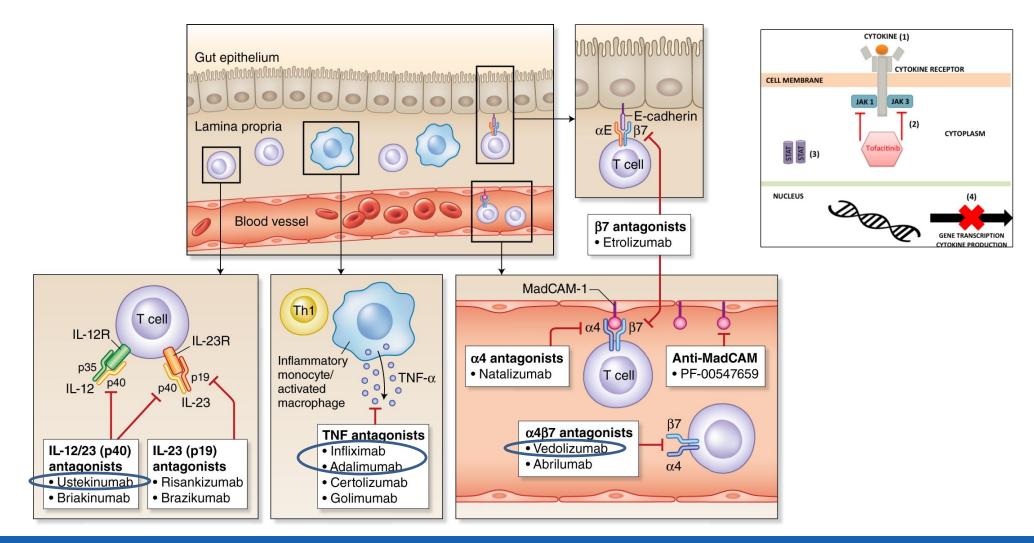


Objectives

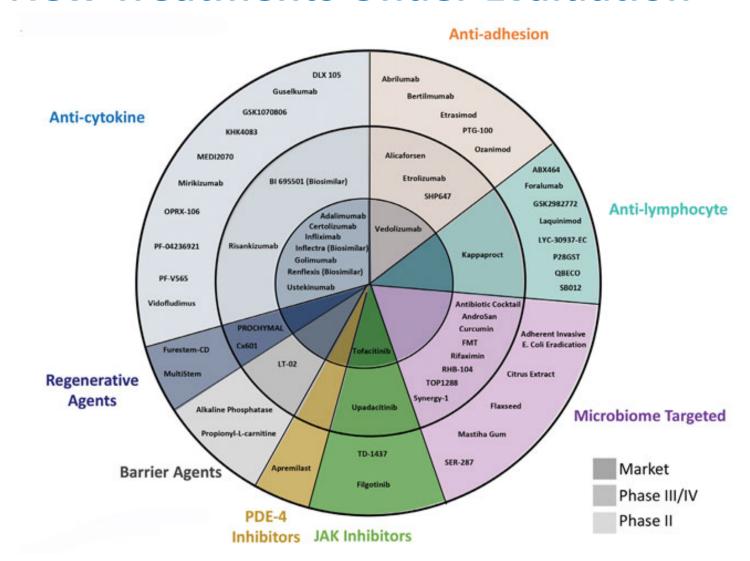
- Review current and future treatment targets in IBD
- Discuss evolving treatment strategies
- Highlight novel non-medication therapies under investigation
- Discuss the role of personalized medicine in IBD therapy



Current Biologic & Small Molecule Therapies for IBD



New Treatments Under Evaluation



IBD Clinical Trials

- As of Feb 2021: >150 Phase I III clinical trials recruiting in the U.S.
 - Phase I: studies assess the safety of a drug
 - Phase II: studies test the efficacy of a drug
 - Phase III: studies involve randomized and blind testing in several hundred to several thousand patients

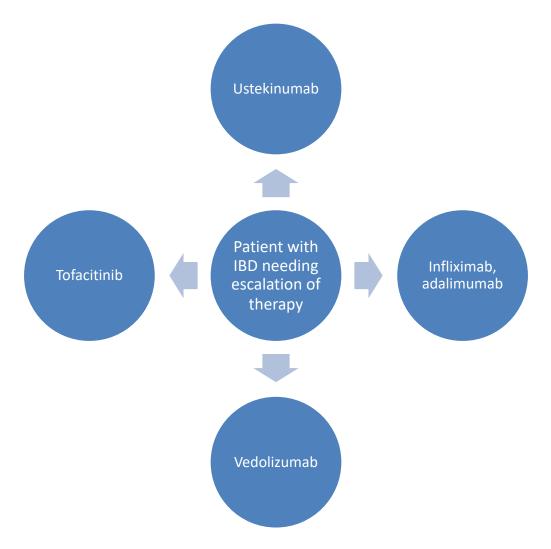


Current Model for Biologic Therapy Selection

Patient Other **Anti-TNF** with new biologic Therapy diagnosis therapies of IBD Patient meets criteria Patient does not for biologic therapy reach remission, loses response or has an adverse response to anti-TNF therapy



Evolving Model for Therapy Selection



Future Model for Therapy Selection



The W's of Evolving IBD Medication Management

 Biologic and small molecule therapies are becoming more readily WHO available for more patients **WHAT** • The number of available therapies is expanding rapidly WHEN • Many patients are getting treated earlier in their disease course WHERE Hospitals and infusion centers, injections, oral medications WHY To reach clinical and endoscopic remission



Beyond Medications

NEW TREATMENT STRATEGIES FOR IBD

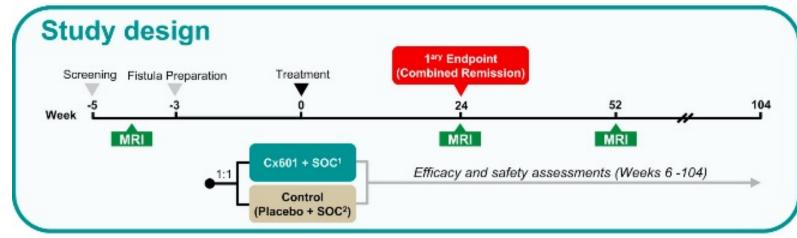


Synbiotics Prebiotic Future Antibiotics **FMT** Diet approaches Current **Probiotics Prebiotics** Standard Tx New human-derived in IBD **LBPs** Clostridium. Well-defined strains Substrates from Protective Pathogenic microbiota species species PolyP, p40, **KFXL** from path E. coli (QBECO) **Editing pathobionts** and inhibiting binding Inflammatory Regulatory Tungstate FimH blocker Bacteriophages - Replace dysbiotic _ pathobionts pathobionts _ pathobionts - | pathobionts microbiota with healthy - ↑ protective species ↑ protective species ↑ protective species protective species AIEC-specific donor's normal microbiome - Modify metabolites † barrier function - ↑ barrier function - † barrier function - 1 pathobionts (bile acid, †SCFA etc.) Modify metabolites - Modify metabolites - Modify metabolites Protective yeasts † protective species (bile acid, ↑SCFA etc.) Modify immunity (bile acid, ↑SCFA etc.) - Modify immunity Corticosteroid Candida glabrata - 1 barrier function (PXR, LTNFα, LII1β etc.) - Modify immunity - Modify immunity - Modify metabolites Thiopurine (↑PPARv, ↑Treg etc.) (†Treg etc.) Engineered bacteria - Modify immunity 5-ASA → • IL-10 IL-35 MTX Potential Agents Potential Agents Potential Agents Potential Agents Potential Agents Ciprofloxacin: Amoxicillin: Saccharomyces boulardii: Inulin; GOS; FOS; GBF; OI; Elemental diet: Fiber: Bank donor/relatives/super JAK-inhibitor BGS; Psyllium; Lactulose; donor FMT: Pre-antibiotics + Metronidazole; Rifamycins; Non-pathogenic Escherichia Mediterranean diet; Asian Anti-IL-12p40 FMT; FMT + prebiotics; Clofazimine: Ethambutol: coli: Lactobacillus reuteri. Fucosyllactose; Yogurt; diet; Semi-vegetarian diet; Anti-TNF-α FMT + prebiotic diet Fosfomycin; Tetracycline; casei, johnsonii, salivarius Glycomacropeptide: Wheat Specific carbohydrate diet; Personalized therapy Anti-integrin bran; Curcumin Clarithromycin; Neomycin; GG: Bifidobacterium longum Fasting-mimicking diet: based on Azithromycin; Combinations Mashiha; Low FODMAP diet Surgery lactis; Clostridium butyricum, microbiota profiles VE202: Firmicutes spore

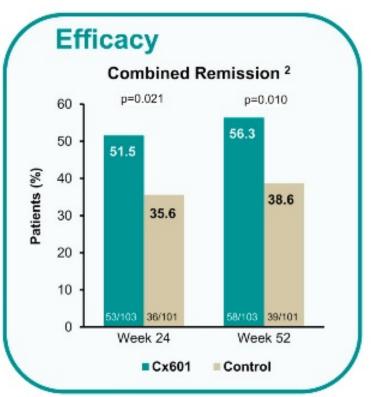
Admire CD Study: Cx601 (darvadatrocel) for Complex Perianal Fistulas in CD (allogeneic adipose-derived stem cells)

Treatment

Cx601 is a suspension of allogeneic expanded adipose-derived stem cells (eASC) injected locally, and has been shown to be efficacious and well tolerated in Crohn's disease patients with treatment-refractory complex perianal fistulas

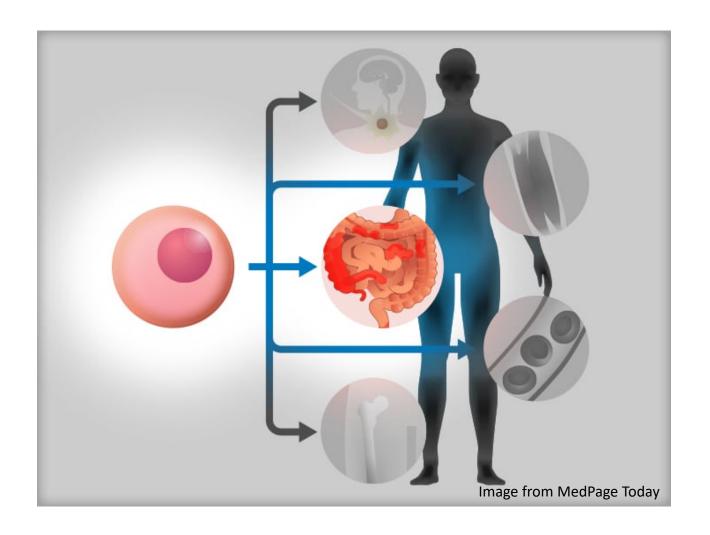






Gastroenterology

Stem Cell Transplantation for Refractory Crohn's Disease







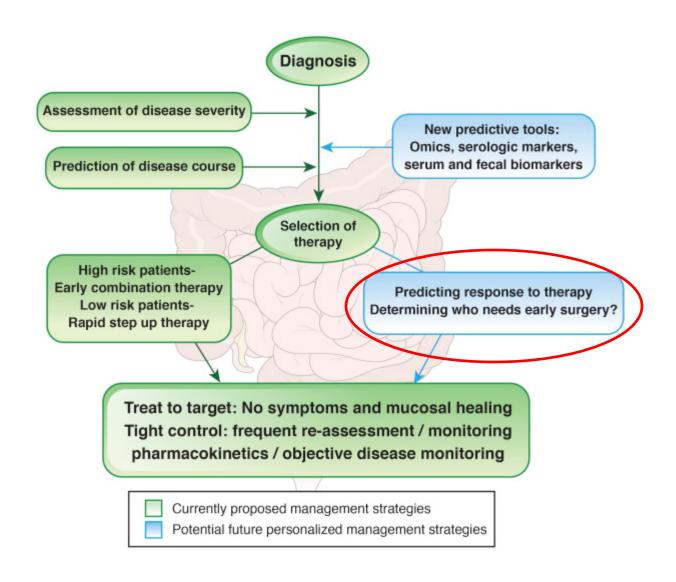


IBD Management in 2021 and Beyond

PERSONALIZED MEDICINE



Prediction of Disease Course to Prioritize Early Anti-TNF Therapy



How Do We Know Who Will Respond?





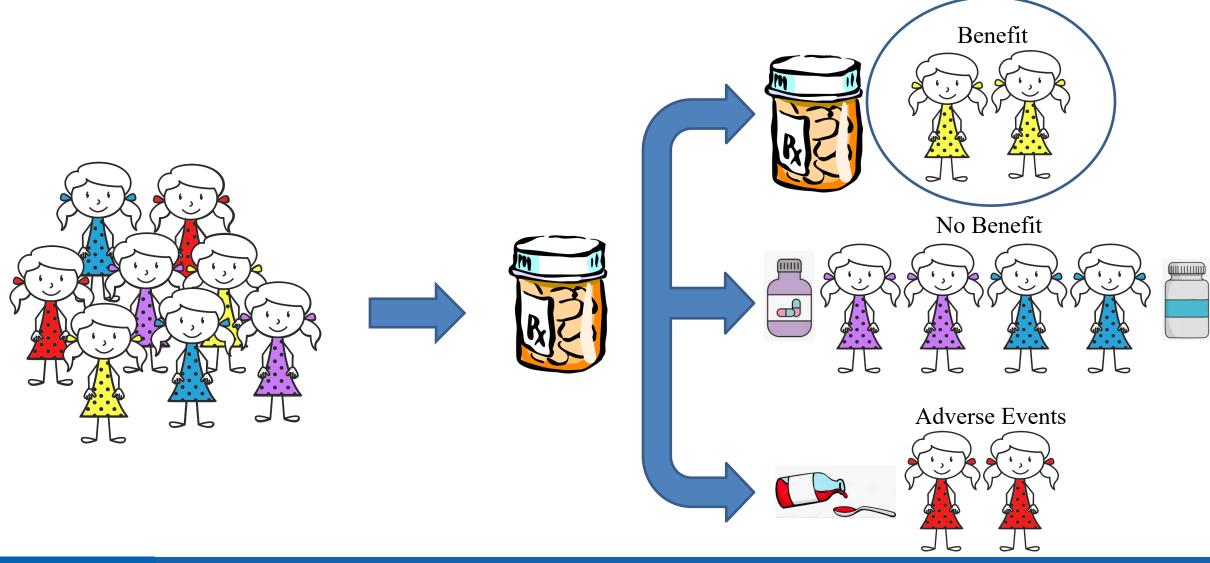
Article

Gene Signatures of Early Response to Anti-TNF Drugs in Pediatric Inflammatory Bowel Disease

Sara Salvador-Martín ^{1,†}, Irene Raposo-Gutiérrez ^{1,†}, Víctor Manuel Navas-López ², Carmen Gallego-Fernández ³, Ana Moreno-Álvarez ⁴, Alfonso Solar-Boga ⁴, Rosana Muñoz-Codoceo ⁵, Lorena Magallares ⁶, Eva Martínez-Ojinaga ⁶, María J. Fobelo ⁷, Antonio Millán-Jiménez ⁸, Alejandro Rodriguez-Martinez ⁹, Concepción A. Vayo ¹⁰, Cesar Sánchez ¹¹, Mar Tolin ¹¹, Ferrán Bossacoma ¹², Gemma Pujol-Muncunill ¹³, Rafael González de Caldas ¹⁴, Inés Loverdos ¹⁵, José A. Blanca-García ¹⁶, Oscar Segarra ¹⁷, Francisco J. Eizaguirre ¹⁸, Ruth García-Romero ¹⁹, Vicente Merino-Bohórquez ²⁰, María Sanjurjo-Sáez ¹ and Luis A. López-Fernández ^{1,*}

Conclusion: Expression of the SMAD7 gene is a pharmacogenomic biomarker of early response to anti-TNF agents in pediatric IBD. TLR2 and DEFA5 need to be validated in larger studies.

Personalized Medicine is the Ultimate Goal



Conclusions

Many new therapies are under investigation

The way we use the current therapies is evolving

The future of IBD therapy is bright

