



Innovative pipeline therapeutics in inflammatory bowel disease: Anti-tumor necrosis factor-like ligand 1A and bispecific antibodies

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There has been significant progress made in inflammatory bowel disease (IBD) over the last couple of decades, with a rapidly increasing number of biologic and small molecules treatments. Coupled with a better understanding of when and how to use treatments appropriately, this has resulted in substantial and meaningful improvement in outcomes for many patients. However, an ongoing issue is that around 30–40% of patients either do not respond or lose response to currently available treatments over time, underscoring the need for further novel therapeutic targets and approaches. Two particularly exciting novel approaches include a novel class of medications targeting tumor necrosis factor-like ligand 1A (TL1A) and the engagement in two pathogenic pathways simultaneously through the use of bispecific antibodies. The development of both of these potential treatment approaches has been built on decades of translational studies, including initial genetic discovery and immune functional validation. The class of molecules targeting TL1A has shown high potency in the pre-clinical setting and emerging data from early-phase interventional clinical trials have been encouraging. Bispecific antibodies have been used so far mostly in the fields of hematology and oncology, but with promising initial findings in IBD that targeting multiple pathways at once, may offer the prospect of greater remission rates or more durable remission than current strategies seeking to target single immunological pathways in isolation. This narrative review presents the latest evidence evaluating TL1A inhibition and bispecific antibodies, including the development pipeline for these molecules as innovative approaches for the next generation of IBD treatments.

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Introduction

There has been significant progress made in inflammatory bowel disease (IBD) over the last couple of decades, with an increasing number of biologic and small molecules treatments becoming available [1,2]. Coupled with a better understanding of when and how to use treatments appropriately, this has resulted in substantial and meaningful improvement in outcomes for patients [3,4]. However, an ongoing issue is that around 30–40% of patients either do not respond or lose response to currently available treatments over time [5–7], underscoring the need for further novel therapeutic targets and approaches [8–10].

In particular, two new strategies offer considerable hope for improved outcomes beyond already existing treatments. This includes targeting both inflammation and fibrosis through inhibition of tumor necrosis factor like-ligand 1A (TL1A), as well as the prospect of targeting more than one key pathogenic pathway through the development of bispecific antibodies. Genetic and translational studies have provided data to support the potential importance of TL1A, with initial encouraging data also seen from interventional clinical trials. Moreover, bispecific antibodies, designed to simultaneously bind two different targets, offer a novel way to address the complex immune pathways involved in immune-mediated disorders like IBD [11]. While most current research on bispecific antibodies has originated from the field of oncology, preclinical research has supported the potential of these molecules to block multiple inflammatory signals at once, such as tumor necrosis factor- α (TNF- α) and interleukin (IL)-23, and several candidates are now advancing through early clinical development in IBD [12]. This narrative review presents the latest evidence evaluating TL1A inhibition and bispecific antibodies as innovative approaches for the next generation of IBD treatments.

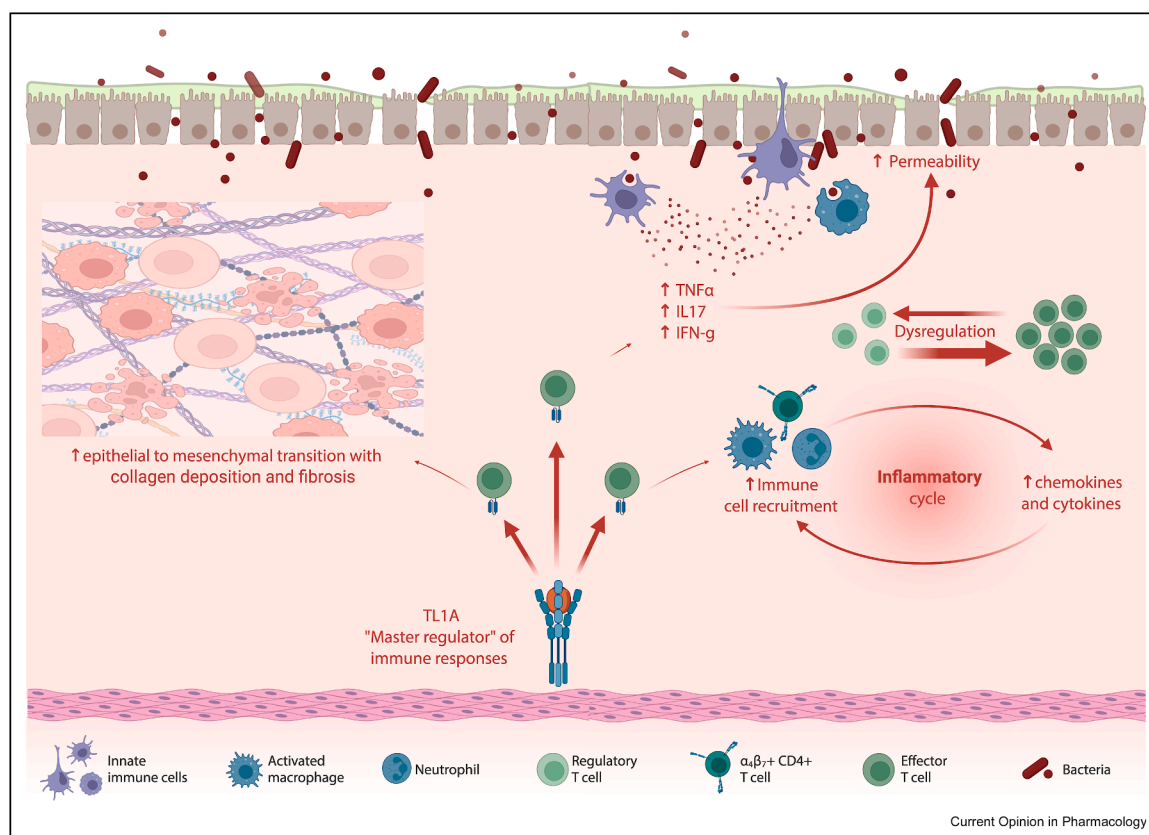
TL1A

TL1A is a member of the TNF superfamily that signals via both death receptor 3 (DR3) and decoy receptor 3 (DcR3), and is thought to play a key role in both mucosal inflammation and fibrosis [13,14]. An initial genome-wide association study identified single nucleotide polymorphisms in the *TNFSF15* gene (encoding for TL1A) and their associations with disease susceptibility [15]. Subsequent work sought to understand the functional consequences of genetic variants in the *TNFSF15* gene, demonstrating this to be an important potential 'master' regulator of mucosal immune responses [16]. Notably, it was discovered that TL1A is normally present in endothelial cells and becomes more active when triggered by inflammatory signals such as TNF- α . Its expression also increases in dendritic cells (DCs) and macrophages following stimulation through toll-like receptors (TLR) such as TLR4 and TLR11, or via interaction with the Fc gamma (Fc γ) receptor [17]. Given such a prominent and ubiquitous role in immune cell activation and inflammation (Figure 1), subsequent pre-clinical and clinical work sought to establish whether targeting TL1A could help in the treatment of IBD.

Pre-clinical studies

In a study using both animal models and human biopsy specimens, TL1A was found to contribute to intestinal inflammation [18]. In mice with chronic dextran sodium sulfate (DSS)-induced colitis, elevated TL1A levels worsened inflammation and were associated with higher expression of T-helper cell 9 (Th9)-related cytokines and transcription factors [18]. Blocking TL1A reduced these effects *in vitro*. Similar patterns were observed in patients with ulcerative colitis (UC), where higher TL1A expression correlated with more severe inflammation and increased Th9 cell markers. In addition, TL1A has been reported to activate the DC-specific intercellular adhesion molecule (ICAM)-grabbing non-integrin-induced RAF1 kinase–NF- κ B pathway. This effect of TL1A, which helps to promote antigen uptake by DCs, has been shown to drive the differentiation of naïve CD4⁺ T cells into Th1 and Th17 subsets, while also synergistically amplifying IL-12-induced IFN- γ and IL-23-induced IL-17 production from these CD4⁺ T cells [19,20]. In addition to its amplification of pro-inflammatory pathways, TL1A has also been linked to fibrosis pathways through immune- and tissue-specific

Figure 1



Targeting TL1A as a potential anti-inflammatory and anti-fibrotic agent. TL1A, tumor necrosis factor-like ligand 1A.

mechanisms. TL1A overexpression *in vitro* in myeloid and lymphoid cells has been shown to increase fibrogenesis, regulated by TNF- α , IL-1 α , and IFN- γ [17]. In parallel, TL1A has also been demonstrated to amplify pro-fibrotic pathways involving IL-17A, IL-13, and especially transforming growth factor-beta (TGF- β). While further work *in vivo* has shown that TL1A-overexpressing mice can develop small bowel wall thickening, particularly in the terminal ileum, with enlarged goblet and Paneth cells, and with muscularis propria hypertrophy [21]. Based on these important laboratory findings, important translational work subsequently demonstrated that blocking TL1A, via neutralizing antibodies or DR3 deletion, can reduce fibroblast and myofibroblast numbers, underscoring its potential role in fibrosis development [22,23]. Subsequent clinical studies have sought to inhibit the TL1A/DR3 pathway in an effort to reduce inflammation and/or fibrosis, while seeking to preserve the TL1A/DcR3 pathway activation, given the recognition of its importance in a range of protective immune pathways.

Clinical studies

Tulisokibart

Tulisokibart (previously named MK-7240 and prior to that PRA-023), an anti-TL1A monoclonal antibody, has shown promising initial efficacy and safety findings as an induction therapy for both UC and Crohn's disease (CD). In the phase 2 ARTEMIS-UC trial, tulisokibart (1000 mg on day 1, followed by 500 mg at weeks 2, 6, and 10) significantly improved clinical remission rates at week 12 compared to placebo (26% vs 2%; $p < 0.001$) [24]. Endoscopic improvement was also more frequent with tulisokibart (37% vs 19%; $p = 0.06$), and the treatment was generally well tolerated with no serious adverse events reported—although over only a short timeframe of a phase 2 induction trial. Similarly, in the phase 2a APOLLO-CD trial [25], tulisokibart (using the same doses and frequencies as the ARTEMIS-UC trial) achieved a significantly higher endoscopic response rate compared to the historical placebo (26% vs 12%; $p = 0.002$) and clinical remission in 49% of patients (vs 16% historically; $p < 0.001$), including those with prior biologic exposure. Reductions in inflammatory biomarkers, such as C-reactive protein and fecal calprotectin have further supported the likely anti-inflammatory effect of this medication. Although early phase 2 findings should be interpreted with some caution, these trials have presented promising data in UC and CD, and further evaluation in phase 3 trials is currently underway in the ongoing ATLAS-UC and ARES-CD trials (NCT06052059 and NCT06430801) as highlighted in Table 1.

Afimbikart

Afimbikart (previously named RO7790121 and prior to that PF-06480605, and prior to that RVT-3101) is

another anti-TL1A molecule that has shown promising findings to date. In the phase 2a single-arm TUSCANY trial, afimbikart demonstrated promising efficacy and an acceptable safety profile in patients with moderate-to-severe UC. Afimbikart (500 mg intravenously every two weeks for a total of seven doses) led to endoscopic improvement in 38% of participants at week 14, significantly exceeding the historical placebo response rate from prior TNF-antagonist-experienced cohorts [26]. Histological outcomes further supported its therapeutic potential, with 33% of patients achieving minimal disease activity based on the Robarts Histopathology Index. Treatment-related adverse events were mostly mild and included, most commonly, disease flare/exacerbation and arthralgia. However, immunogenicity was a notable concern in this trial, with anti-drug antibodies reported in 82% of participants, although the presence of neutralizing antibodies, which are perhaps of most significance, was much less at 10%. The results from the ongoing phase 3 AMTERINE-UC trial in UC and the phase 2 TAHOE trial in CD (Figure 1) are awaited.

Duvakitug

Duvakitug (formerly named TEV-48574) is another anti-TL1A molecule undergoing evaluation in clinical trials. The evaluation of duvakitug is particularly exciting given recent interest in bringing master-protocol approaches to the field of IBD, to speed up drug development [27–29]. A phase 2 basket trial of duvakitug in UC and CD is currently ongoing, called RELIEVE UCCD. This is a double-blind, placebo-controlled, international basket trial evaluating placebo vs a 450 mg dose vs a 900 mg dose and seeking to assess endoscopic response at week 14, with the use of both Bayesian and frequentist statistical analyses. Initial findings from both the UC and CD baskets have been highly promising, with a high posterior probability of efficacy for both the lower (450 mg) dose and the higher (900 mg) dose in both UC and CD [30,31].

The relevant doses of current anti-TL1As in late-phase testing have been summarized in Table 2. In addition, there are several further anti-TL1A molecules in early-phase development. Other anti-TL1A molecules under investigation include, but are not limited to, FG-M701, SPY002-091 & SPY002-072, XmAb942, and ABS-101. These molecules are currently at much earlier stages in the drug development lifecycle, and clinical trial data are currently awaited from these drug development programs.

There has been notable interest in applying precision medicine approaches in IBD, but to date, little success has been achieved in this regard [32]. Therefore, an important additional aspect of the TL1A development program is the potential of this pathway and these molecules to be accompanied by the first 'companion

Table 1

Key drug development programs for bispecific antibodies and tumor necrosis factor-like cytokine 1A (TL1A) inhibitors.

		Pre-clinical	Phase 1	Phase 2	Phase 3
Bispecific antibodies	MTX-201 (binds inhibitory KIR and ICOS of CD8 Treg)		NCT06080048	To be launched	
TL1A inhibitors	SOR102 (anti-IL-23p19 + TNF- α)				
	Afirmkibart			TUSCANY-1 and TUSCANY-2 (UC) TAHOE (CD) – started in July 2023	Ongoing - NCT06588855 and NCT06589986 (AMETRINE-1 and AMETRINE-2, UC), and NCT06819878 (SIBERITE-1, CD)
	Tulisokibart			ARTEMIS (UC) and APOLLO (CD)	Ongoing - NCT06052059 (ATLAS-UC, UC) and NCT06430801 (ARES-CD, CD); long-term extension (NCT06651281) Anticipated to start in late 2025
	Duvakitug			RELIEVE UCCD (UC and CD)	
	BCD-261		NCT06715540	COMANDOR (CD) - started in August 2025	
	VIAL-TL1A-HLE (subcutaneous, extended half-life)		BB-TL1A-1.0 (HC and UC) - started in June 2025		

NCT, clinical trial identifier; CD, Crohn's disease; HC, healthy controls; IBD, inflammatory bowel disease; ICOS, inducible T-cell co-stimulator; TNF- α , tumor necrosis factor-alpha; Treg, regulatory T cell; TL1A, tumor necrosis factor-like cytokine 1A; UC, ulcerative colitis.

diagnostic' precision medicine test in IBD [24]. This companion diagnostic is a genetic test that was developed using machine learning approaches and is composed of several key polymorphisms with relevant weighting applied. It is notable that this companion biomarker is being incorporated into ongoing anti-TL1A trial programs, although initial readouts from the phase 2 setting have been equivocal [24]. Assessment, particularly in the phase 3 clinical trial setting, should help determine whether biomarker-guided treatment can demonstrate utility, and even if utility is not demonstrated, it is hoped that there would still be helpful insights provided into future precision medicine approaches in IBD [33].

It is currently not clear what role (if any) the anti-TL1As will have in treating extra-intestinal manifestations of IBD, but this is an important area of unmet need where these molecules may also be applied [34,35]. Rather than the explanatory trials of drug development programs, it is most likely that such answers about treatment strategy will be best achieved through pragmatic, investigator-led treatment strategy trials after licensing of the above medications [36–38].

Bispecific antibodies

The challenge of achieving higher remission rates and more durable remission in IBD has sparked growing interest in combining therapies with different mechanisms of action (advanced combination therapies), including biologics with different mechanisms of action, or combining a biologic plus a small molecule [39–41]. A further, perhaps more innovative, development in this space is the potential to use bispecific antibodies (BsAbs) as an alternative mechanism to provide advanced combination therapy. This is especially attractive due to the multiple immune pathways known to play a role in IBD. BsAbs are engineered molecules capable of binding two distinct antigens or epitopes and broadly fall into two broad categories: those resembling Immunoglobulin (Ig)G antibodies with an Fc region that allows immune system interaction and those without Fc regions, which work purely through antigen binding [42,43]. Some BsAbs are designed to block redundant ligands, while others simultaneously bind two separate targets on the same or different immune pathways. Interestingly, it has been proposed that these molecules may have biological activity not seen when using solely the 'parent antibodies' in isolation [42].

Table 2

Summary of clinical studies of tumor necrosis factor-like cytokine 1A (TL1A) inhibitors in ulcerative colitis and Crohn's disease.

Drug	Disease	Study name and ID	Study design	Patient characteristics	Dosage regimens	Efficacy	Safety
Afimkibart [26]	UC	TUSCANY -NCT04090411	Double-blind, treat-through, placebo-controlled, multi-dose, induction and maintenance trial	Adults (18–75 years) with moderate-to-severe UC (total Mayo score 6–12, endoscopic subscore ≥ 2)	Nine treatment groups: SC afimkibart 50 mg, 150 mg, 450 mg, or matched placebo every 4 weeks during the 12-week induction period; SC afimkibart 50 mg, 150 mg, or 450 mg during the treat-through 40-week maintenance period	At week 14, clinical remission by total Mayo score occurred in 26%, 23%, and 24% receiving afimkibart 50 mg, 150 mg, and 450 mg, respectively, vs 12% with placebo ($p > 0.05$). Using the modified Mayo score, remission rates were higher - 30%, 35%, and 32% for afimkibart 50 mg, 150 mg, and 450 mg, respectively, vs 12% with placebo statistically significant differences (risk differences 18.2–23.4%, 90% CIs all above 0).	Treatment-emergent adverse events occurred in 48% of patients during induction and 59% during maintenance with overall incidences similar to placebo; the most common were nausea, urinary tract infection, anemia, and fatigue.
Tulisokibart [24]	UC	ARTEMIS - NCT04996797	Double-blind, placebo-controlled, induction trial	Adults (≥ 18 years) with moderately to severely active UC; prior glucocorticoid dependence or failure of conventional or AT; disease extent ≥ 15 cm; baseline modified Mayo score 4–9; approximately half had prior biologic exposure	Tulisokibart 1000 mg IV on day 1, then 500 mg IV at weeks 2, 6, 10 vs placebo	Clinical remission occurred in 26% (tulisokibart) vs 1% (placebo; $p < 0.001$). Endoscopic improvement was 37% vs 6% ($p < 0.001$), and clinical response 66% vs 22% ($p < 0.001$). Symptomatic remission (19% vs 6%; $p = 0.02$), histologic and mucosal improvements (31–46% vs 4–18%; $p < 0.001$), and IBDQ response (82% vs 49%; $p < 0.001$) all favored tulisokibart. Results were consistent across subgroups, including prior biologic exposure and concomitant steroid or immunosuppressant use.	Adverse events: 46% (tulisokibart) vs 43% (placebo); serious AEs 1% vs 8%; infections 18% each group. No infusion reactions.

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Table 2. (continued)

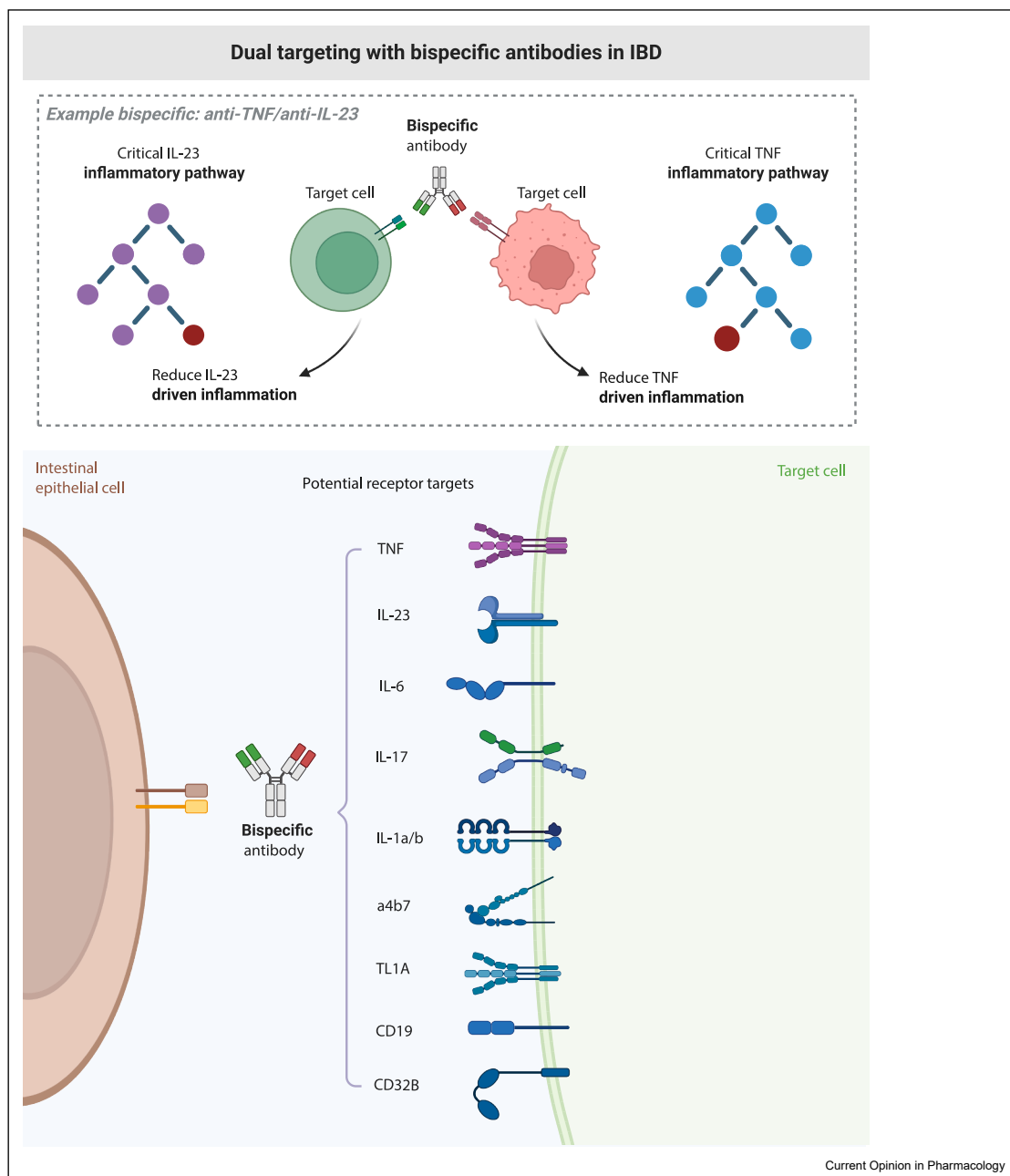
Drug	Disease	Study name and ID	Study design	Patient characteristics	Dosage regimens	Efficacy	Safety
Tulisokibart [25]	CD	APOLLO - NCT05013905	Open-label, induction study using historical placebo estimates as comparator	Adults with moderately to severely active Crohn's disease (CDAI $\geq 220 \leq 450$, SES-CD ≥ 6 or ≥ 4 for isolated ileal disease); permitted concomitant steroids or immunosuppressants	Tulisokibart 1000 mg IV day 1, then 500 mg IV at weeks 2, 6, and 10	Endoscopic response: 26% vs 12% (historical placebo; $p = 0.002$). Clinical remission (CDAI < 150): 49% vs 16%; $p < 0.001$. Biologic-exposed subgroup: 33% endoscopic response, 38.5% clinical remission. Significant reductions in CRP and faecal calprotectin at all timepoints.	Tulisokibart was well tolerated. 46% reported mild/moderate infections; two serious infections were unrelated and resolved. At week 50, infection occurred in 63% (100 mg) and 61% (250 mg) groups, none serious. No dose-dependent safety signals.
Duvakitug [31]	UC	RELIEVE UCCD - NCT05499130	Double-blind, placebo-controlled, dose-ranging, induction study (basket trial)	Adults with moderate-to-severe UC and inadequate response, loss of response, or intolerance to conventional or AT; prior AT-experienced and AT-naïve participants included	Duvakitug 2250 mg SC day 1 > 450 mg SC or 900 mg SC every 2 weeks vs placebo	Clinical remission (modified Mayo) at week 14: 36% (450 mg) and 48% (900 mg) vs 20% (placebo); placebo-adjusted rates +16 % (450 mg), +27% (900 mg); both doses statistically significant with > 0.90 posterior probability of superiority ($p < 0.05$). Treatment effect consistent across AT-experienced and -naïve subgroups.	Adverse events: 49% (450 mg), 43% (900 mg), 52% (placebo); AEs leading to discontinuation: 0% (450 mg), 2% (900 mg), 5% (placebo). No new safety signals observed; duvakitug was well tolerated.
Duvakitug [30]	CD	RELIEVE UCCD - NCT05499130	Double-blind, placebo-controlled, dose-ranging, induction study (basket trial)	Adults with moderate-to-severe CD and inadequate response, loss of response, or intolerance to conventional or AT; prior AT-experienced and AT-naïve participants included	Duvakitug 2250 mg SC day 1 > 450 mg SC or 900 mg SC every 2 weeks vs placebo	Primary endpoint (week 14 endoscopic response $\geq 50\%$ SES-CD reduction): 26% (450 mg) and 48% (900 mg) vs 13% (placebo); placebo-adjusted +13 pp (450 mg) and +35 pp (900 mg); statistically significant with > 0.90 posterior probability of superiority ($p < 0.05$). Efficacy consistent across AT-experienced and AT-naïve subgroups.	Adverse events: 67% (450 mg), 43% (900 mg), 48% (placebo). AEs leading to discontinuation: 9% (450 mg), 2% (900 mg and placebo). Duvakitug was well tolerated.

AE, adverse event; AT, advanced therapy; CD, Crohn's disease; CDAI, Crohn's Disease Activity Index; CI, confidence interval; CRP, C-reactive protein; IV, intravenous; IBDQ, inflammatory bowel disease questionnaire; mg, milligram; OLE, open-label extension; PBO, placebo; pp, percentage points; SC, subcutaneous; SES-CD, simple endoscopic score for Crohn's disease; UC, ulcerative colitis; vs, versus.

Most of the clinical development of BsAbs to date has focused on hematological and oncological malignancies. Indeed, since 2014, a few BsAbs have already been licensed, including: blinatumomab, emicizumab, amivantamab, faricimab, and glofitamab. Outside hematology and oncology, progress has been slower, however, BsAbs are now being studied for their potential across immune-mediated inflammatory diseases (IMIDs) [44]. One notable example from the field of IMIDs is sonelokimab, a BsAb targeting IL-17A and IL-17F, which

has emerged as a novel therapeutic candidate for psoriasis, psoriatic arthritis, and hidradenitis suppurativa [45]. There have been highly promising findings from phase 2 trials, with results from ongoing phase 3 trials being eagerly awaited. For IBD, although the evidence base is more limited, the rationale for the use of BsAbs is similar [46,47]. Targeting multiple inflammatory mediators, like TNF, IL-12/23, and $\alpha 4\beta 7$ integrin, with a single agent could help overcome some of the limitations seen with currently available monotherapies (Figure 2).

Figure 2



Bispecific antibodies and potential for application in IBD. IBD, inflammatory bowel disease.

Preclinical studies

Preclinical studies have started to validate this concept. In a recent study, Yin et al. evaluated a bispecific antibody (named FL-BsAb1/17) that targets IL-1 β and IL-17A in a mouse model of colitis induced by 3% dextran sulfate [48]. When compared to etanercept, a TNF- α inhibitor, FL-BsAb1/17 was more effective in relieving mouse symptoms and signs of inflammation. It also suppressed a range of inflammatory markers in serum and colonic tissue, including IL-1 β , IL-6, IL-12, IL-22, IL-23, and TNF- α [48]. These findings suggest that dual inhibition of inflammatory cytokines may be more effective than single-cytokine approaches in controlling intestinal inflammation. An additional factor to consider, though, is that the design and structure of BsAbs can be incredibly diverse, with platforms that allow developers to tailor antibodies for valency, affinity, and molecular architecture [42]. However, this flexibility could prove valuable in IBD, where the ideal therapeutic profile might require fine-tuning to balance efficacy with safety—and may vary between individual patients.

Clinical studies

Although clinical experience with BsAbs in IBD is still limited, several promising candidates are moving through clinical trial development programs. Lutikizumab (previously known as ABT-981) is a bispecific antibody which binds both IL1- α and IL1- β and has shown promise across a range of IMIDs, and is now under investigation in both CD in the phase 2 TARGET CD trial (NCT06548542) and in UC in the phase 3 HORIZON trial (NCT06257875). In addition, another molecule, SOR102, consists of V900, a humanized llama-derived domain antibody targeting the p19 subunit of IL-23. It is also engineered for resistance to intestinal proteases, fused with V565, a previously characterized domain antibody against TNF- α . The two domains are linked via a central protease-cleavable linker, forming a single molecule designed for oral administration. This molecule is currently being tested in a phase I trial for both healthy volunteers and patients with UC. The phase I trial is seeking to assess safety, tolerability, and pharmacokinetics using ascending doses. Initial findings suggest that SOR102 has a manageable safety profile and favorable pharmacodynamics, though more data are expected soon [12].

Several further BsAbs are in preclinical stages, including bispecific antibodies for IL-23 and TL1A [49]. However, it is important to note that there are multiple unknowns with regards BsAbs compared to single-target biological therapies, including ratios of target binding, the duration of target binding, whether the use of higher-molecular weight BsAbs may actually increase immunogenicity, as well as unknowns regarding long-term safety implications. A particular concern exists around higher levels of immunosuppression with bispecific antibodies. Much like the investigation of infection and malignancy risk

with ‘classical’ combination therapies in IBD, the longer-term risk of bispecific antibodies will likely become clearer with adequately designed, large, prospective, registry-based studies focusing on safety. Given the growing number of BsAbs under investigation, and their potential added complexities, the United States Food and Drug Administration has issued specific guidance for sponsors to assist with navigating regulatory requirements for the investigation of BsAbs [50].

An additional unknown at this stage is where anti-TL1A molecules and BsAbs would sit within the therapeutic landscape for the management of CD and UC. Although increasing treatment options are certainly welcome, they do come with an added complexity regarding treatment selection decisions for patients and clinicians [2]. Clinical trials of treatment strategies determining how and when to most optimally use these medications are likely to play a pivotal role [36], coupled with longer-term data, cost-effectiveness analyses, and large, well-conducted, prospective ‘real-world’ studies.

Conclusions

Despite much progress in the management of IBD, there still remain many areas of unmet need for patients. However, the pipeline for innovative approaches is rich, and there is considerable promise for the anti-TL1A class of molecules as potential new treatments for both UC and CD. Additionally, bispecific antibodies also offer significant potential as novel therapeutic approaches to safely and effectively deliver ‘combination therapy’ in IBD. Despite substantial hope, the clinical utility of these treatment strategies will ultimately depend on their demonstrating clear advantages over existing treatments in terms of medium- and long-term efficacy and safety (with regard to immune complex formation and immunogenicity). Ultimately, practical considerations such as dosing, manufacturing scalability, and cost-effectiveness will be key to determine where these new molecules will likely fit into future clinical practice.

Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: MME has received speaker fees from J&J, outside the submitted work. NMN has received personal fees/grants from AbbVie, BMS, Celltrion, Dr Falk, J&J, Lilly, Medfyle, Pfizer, Pharmacosmos, Takeda, Tillotts, outside the submitted work.

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