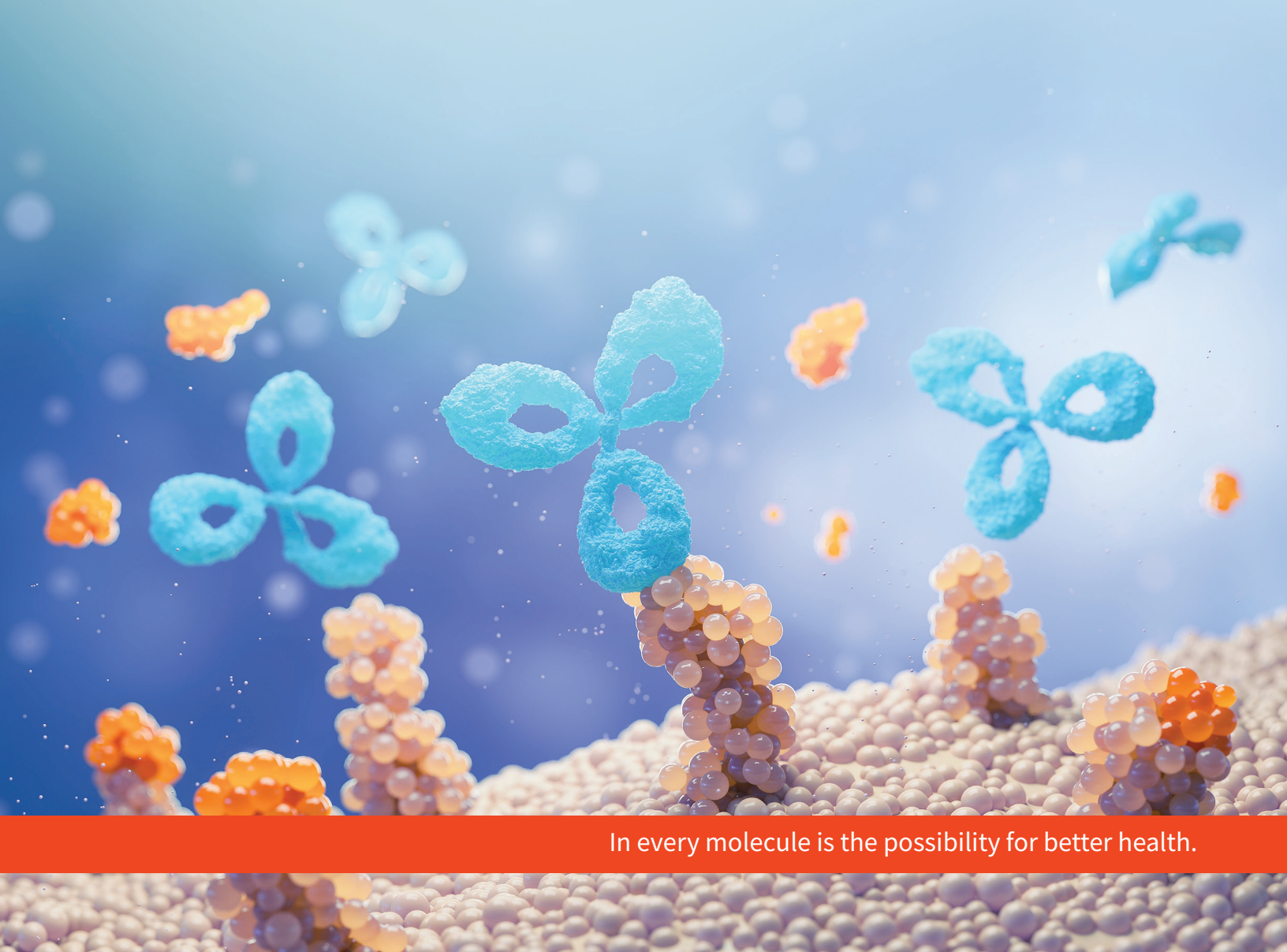


Case Study

Effect of 5-FU and Bevacizumab on a Colon Cancer PDX Model in Female NOD SCID Mice



In every molecule is the possibility for better health.

Overview

Patient-derived xenograft (PDX) models are widely employed in oncology drug development due to their ability to preserve the histological, molecular, and pharmacological characteristics of the original patient tumor. Colorectal cancer is one of the leading causes of cancer-related mortality worldwide, and KRAS mutations are among the most frequently observed genetic alterations associated with disease progression and therapeutic response.

In this study, the antitumor efficacy of 5-fluorouracil (5-FU) alone and in combination with bevacizumab was evaluated in a colon cancer PDX model harboring a KRAS G12V Tier 1 mutation. The study assessed tumor growth inhibition, tolerability, and histopathological changes following treatment in female NOD SCID mice bearing established colon PDX tumors.

Aragen’s Approach

Model Details

Parameter	Description
Tumor Model	Colon PDX
Mutation Status	KRAS G12V (Tier 1 mutation)
Host Animals	Female NOD SCID mice
Group Size	n=6 animals/group

Treatment Groups

Group	Treatment
G1	Vehicle
G2	5-FU (50 mg/kg, IP, twice weekly)
G3	5-FU (50 mg/kg, IP, twice weekly) + Bevacizumab (5 mg/kg, IP, twice weekly)

Study Timeline

- **Day -19:** PDX tumor implantation
- **Day 0-33:** Treatment period
- **Day 33:** Study termination

Outcomes

Tumor Growth Inhibition

Vehicle-treated animals showed rapid and progressive tumor growth, reaching a mean tumor volume of approximately 1,000 mm³ by Day 33. In contrast, treatment with 5-FU significantly slowed tumor progression, while the combination of 5-FU and bevacizumab produced the greatest antitumor effect throughout the study (Figure 1).

- **5-FU monotherapy** reduced tumor growth compared with vehicle controls.
- **5-FU + Beacizumab** consistently maintained the lowest tumor volumes, demonstrating superior efficacy over 5-FU alone.
- The treatment effect became more pronounced over time, with the combination group showing an earlier onset and greater magnitude of tumor growth suppression.

Statistically significant differences (Two-way Anova) were observed between:

- **Vehicle vs. 5-FU:** Days 22–33
- **Vehicle vs. 5-FU + Bevacizumab:** Days 19–33, indicating an earlier treatment response with combination therapy

Treatment with 5-FU significantly inhibited tumor growth, while the addition of bevacizumab further enhanced antitumor activity, resulting in earlier and greater tumor growth suppression than chemotherapy alone. These findings highlight the potential therapeutic benefit of combining anti-angiogenic therapy with standard chemotherapy in this KRAS G12V-mutant colon PDX model.

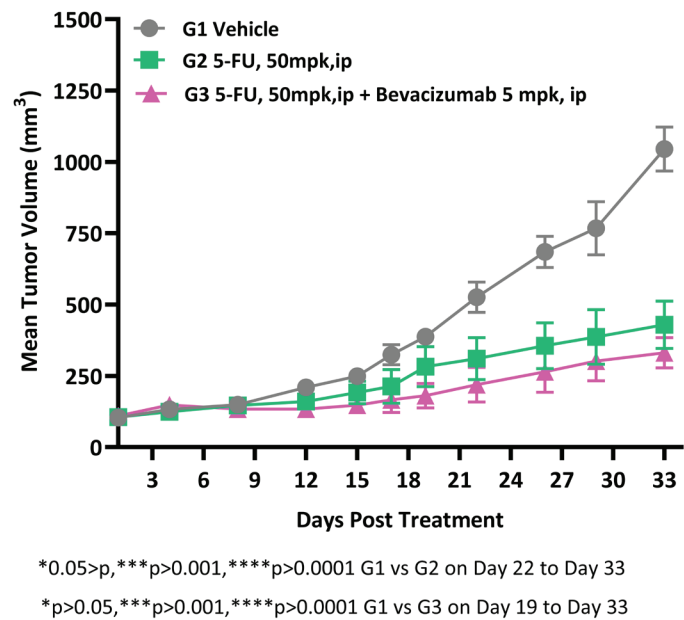
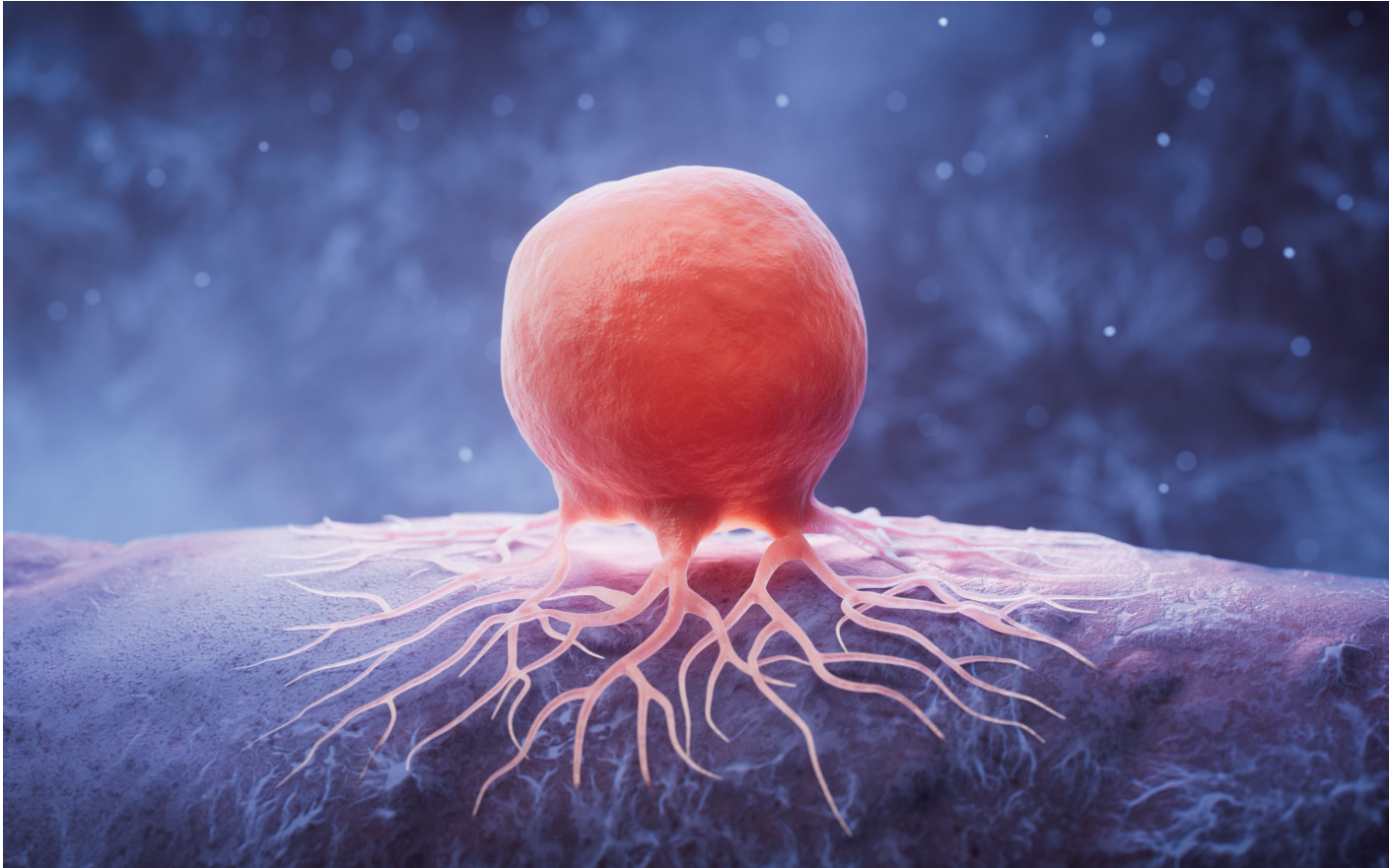


Figure 1: Tumor Growth Inhibition. Mean tumor volume progression in female NOD SCID mice bearing a KRAS G12V-mutant colon patient-derived xenograft (PDX) following treatment with vehicle, 5-FU (50 mg/kg, IP), or 5-FU (50 mg/kg, IP) in combination with bevacizumab (5 mg/kg, IP). The combination therapy demonstrated earlier and greater tumor growth suppression than 5-FU monotherapy. Data are presented as mean ± SEM. Statistical significance (Two-way Anova) was observed for Vehicle vs. 5-FU from Days 22–33 and Vehicle vs. 5-FU + Bevacizumab from Days 19–33.



Tolerability Assessment

Body weight was monitored throughout the study as an indicator of treatment-related toxicity. Overall, both 5-FU monotherapy and 5-FU plus bevacizumab combination therapy were generally well tolerated, with animals maintaining stable body weight profiles throughout the study (Figure 2).

- Transient decreases in body weight were observed during the early treatment phase; however, animals recovered rapidly and returned to near-baseline body weights.
- No treatment group exhibited sustained or severe body-weight loss, indicating an acceptable safety profile.
- Body weight fluctuations remained within acceptable limits and did not suggest cumulative toxicity.
- The addition of bevacizumab did not result in appreciable additional toxicity compared with 5-FU monotherapy.

Importantly, the enhanced antitumor activity observed with the 5-FU and bevacizumab combination was achieved without increased systemic toxicity, supporting a favorable therapeutic benefit–risk profile in this KRAS G12V-mutant colon PDX model.

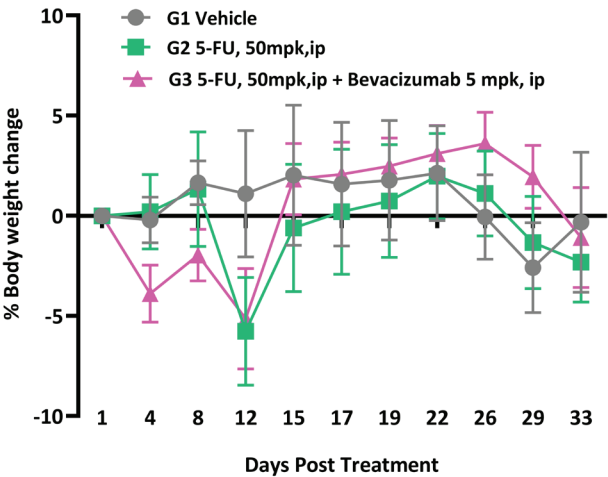


Figure 2: Tolerability Assessment. Percentage body weight change in female NOD SCID mice bearing a KRAS G12V-mutant colon PDX following treatment with vehicle, 5-FU (50 mg/kg, IP), or 5-FU (50 mg/kg, IP) in combination with bevacizumab (5 mg/kg, IP). Both treatment regimens were well tolerated, with no sustained or severe body weight loss observed during the study. Data are presented as mean ± SEM.

Histopathological Evaluation

H&E staining was performed on tumor tissues collected at study termination.

Histopathology Scores

Parameter	Vehicle (G1)	5-FU (G2)	5-FU + Bevacizumab (G3)
Glandular Differentiation	1	1	1
Nuclear Atypia	2	2	2
Mitotic Activity	3	1	0
Tumor Necrosis (%)	3	1	2
Stromal Reaction/Desmoplasia	2	2	1
Total Score	11	7	5

Histological Findings

Histopathological evaluation revealed marked treatment-associated changes in the tumor tissues.

Compared with vehicle controls:

- 5-FU treatment reduced mitotic activity, indicating decreased tumor cell proliferation.
- The combination of 5-FU and bevacizumab further reduced mitotic activity, achieving a score of zero.
- Lower overall histopathology scores were observed in treated groups, with the combination therapy exhibiting the lowest total score (5) versus vehicle (11).

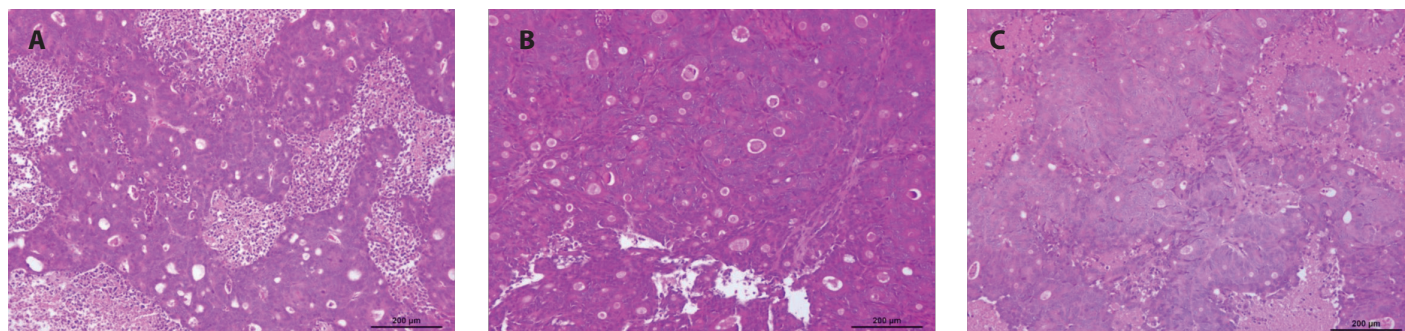


Figure 3: Representative images from H&E staining (100X) of excised tumor sections from G1: Vehicle (A), G2: 5-FU 50mpk, ip (B) and G3: 5-FU 50mpk, i.p. + Bevacizumab 5 mpk, i.p.

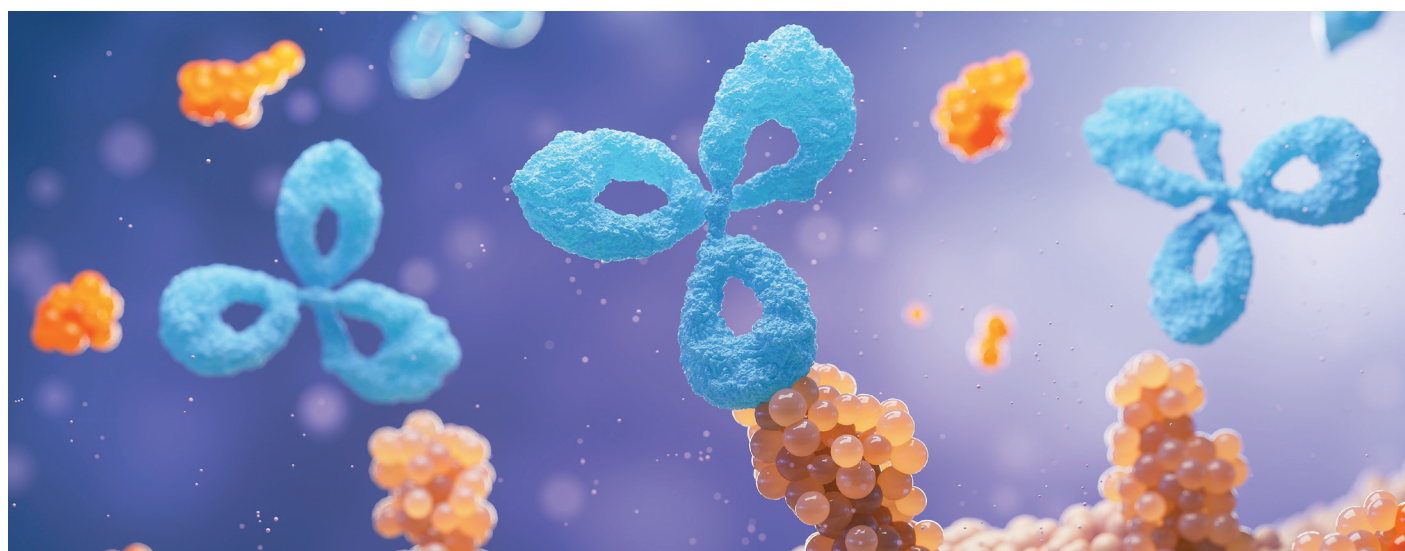
Representative H&E staining results (Figure 3) demonstrated reduced tumor cellularity and treatment-related morphological alterations in the combination group relative to controls.

These findings corroborate the observed antitumor efficacy and suggest enhanced suppression of tumor progression following combination therapy.

Conclusion

In a KRAS G12V-mutant colon cancer PDX model, 5-FU significantly inhibited tumor growth, while the addition of bevacizumab delivered earlier and greater tumor growth suppression. The combination therapy was well tolerated and did not result in additional systemic toxicity. Histopathological findings further supported the efficacy data, demonstrating reduced mitotic activity and the lowest overall pathology score in the combination group.

Collectively, these results highlight the therapeutic benefit of combining 5-FU with bevacizumab and demonstrate the value of this PDX model for evaluating colorectal cancer treatment strategies. To further elucidate treatment response, Aragen can support translational characterization of this model through immunohistochemistry (IHC) and downstream biomarker analyses, including Ki67, p53, CDX2, CK20, and EpCAM, providing deeper mechanistic insights and supporting biomarker target-driven efficacy assessment.



Why Aragen?

Aragen provides an integrated **in vivo oncology platform** that supports oncology drug discovery from efficacy evaluation to translational insights.

- **Robust tumor model portfolio** including human xenograft, syngeneic, orthotopic, dispersed, and subcutaneous models across multiple cancer types.
- **Advanced in vivo imaging** (BLI, FLI, X-ray) for real-time monitoring of tumor growth, metastasis, and therapeutic response.
- **Comprehensive bioanalysis and PK/PD correlation** to connect drug exposure with efficacy outcomes.
- **Integrated histopathology and biomarker analysis** (MSD, ELISA, HTRF, FACS, qPCR) for deeper mechanistic understanding.
- **Hematology, clinical chemistry, and toxicity assessment** to enable simultaneous evaluation of efficacy and safety.
- **End-to-end translational support** that helps accelerate informed decision-making throughout preclinical development.

From tumor model selection to biomarker-driven insights, Aragen delivers comprehensive oncology solutions to support confident go/no-go decisions.

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At Aragen, we recognize your work is vital, urgent and impacts lives. Our purpose, 'In every molecule is the possibility for better health' motivates us to drive the success of your programs, so that we can together transform hope into health for millions of people around the world.

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