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内容：潰瘍性大腸炎において IL-23p19 阻害薬リサンキズマブは臨床的寛解率を改善する

出典：Risankizumab for Ulcerative Colitis: Two Randomized Clinical Trials. JAMA. 2024 Jul 22; pii: e2412414.

https://pubmed.ncbi.nlm.nih.gov/39037800/

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リサンキズマブは、尋常性乾癬、乾癬性関節炎、およびクローン病の治療に使用されるインターロイキン 23A を標的とするヒト化モノクローナル抗体です。中等症～重症の活動期潰瘍性大腸炎患者において、リサンキズマブは寛解導入療法および維持療法として、プラセボと比較し臨床的寛解率を改善するか、ベルギー・リエージュ大学病院の INSPIRE and COMMAND Study Group が、第 III 相無作為化二重盲検プラセボ対照試験「INSPIRE 試験」および「COMMAND 試験」の結果を JAMA 誌オンライン版 2024 年 7 月 22 日号に報告した。

導入療法試験「INSPIRE 試験」は、2020 年 11 月 5 日～2022 年 8 月 4 日に 41 ヵ国 261 施設で実施された。患者 977 例を、リサンキズマブ（1,200mg）群またはプラセボ群に 2 対 1 の割合で無作為に割り付け、0 週、4 週および 8 週に静脈内投与した。主要アウトカムの 12 週時の臨床的寛解率は、リサンキズマブ群 20.3%（132/650 例）、プラセボ群 6.2%（20/325 例）であった（補正後群間差：14.0%、95%信頼区間[CI]：10.0～18.0、p＜0.001）。

維持療法試験「COMMAND 試験」は、2018 年 8 月 28 日～2022 年 3 月 30 日に 37 ヵ国 238 施設で実施された。584 例を、リサンキズマブ 180mg 群、360mg 群またはプラセボ群に 1 対 1 対 1 の割合で無作為に割り付け、8 週ごとに 52 週にわたり皮下投与した。主要アウトカムの 52 週時の臨床的寛解率は、リサンキズマブ 180mg 群 40.2%（72/179 例）、リサンキズマブ 360mg 群 37.6%（70/186 例）、プラセボ群 25.1%（46/183 例）であった。リサンキズマブ 180mg 群とプラセボ群の補正後群間差は 16.3%（97.5%CI：6.1～26.6、p＜0.001）、リサンキズマブ 360mg 群とプラセボ群の補正後群間差は 14.2%（4.0～24.5、p＝0.002）であった。

Table 2. Primary and Key Secondary Outcomes in the Induction Trial

	No. (%) [95% CI][a]		Adjusted between-group difference, % (95% CI)[b]	P value[c]
	1200 mg of risankizumab administered intravenously (n = 650)	Placebo administered intravenously (n = 325)		
Primary outcome				
Clinical remission (determined using the adapted Mayo score)[d,e]	132 (20.3) [17.2 to 23.4]	20 (6.2) [3.6 to 8.9]	14.0 (10.0 to 18.0)	<.001
Secondary outcomes				
Clinical response[f]				
Determined using the adapted Mayo score[g]	418 (64.3) [60.6 to 67.9]	116 (35.7) [30.5 to 40.9]	28.6 (22.3 to 34.8)	<.001
Determined using the partial adapted Mayo score at wk 4[g]	339 (52.2) [48.3 to 56.0]	99 (30.5) [25.5 to 35.5]	21.8 (15.6 to 28.1)	<.001
Improvement				
Endoscopic[h]	237 (36.5) [32.8 to 40.2]	39 (12.1) [8.5 to 15.6]	24.3 (19.3 to 29.4)	<.001
Histological, endoscopic, and mucosal[i]	159 (24.5) [21.2 to 27.8]	25 (7.7) [4.8 to 10.6]	16.6 (12.3 to 21.0)	<.001
Endoscopic remission[j]	69 (10.6) [8.2 to 13.0]	11 (3.4) [1.4 to 5.4]	7.2 (4.2 to 10.2)	<.001
No bowel urgency[k]	287 (44.1) [40.3 to 47.9]	90 (27.7) [22.8 to 32.6]	16.3 (10.3 to 22.4)	<.001
No abdominal pain[k]	232 (35.8) [32.1 to 39.4]	86 (26.5) [21.7 to 31.3]	9.3 (3.4 to 15.3)	.002
Histological, endoscopic, and mucosal remission[l]	41 (6.3) [4.4 to 8.2]	2 (0.6) [0 to 1.5]	5.6 (3.5 to 7.7)	<.001
Mean change (95% CI)				
13-Item Functional Assessment of Chronic Illness Therapy-Fatigue scale score[m]	7.9 (7.0 to 8.7)	3.3 (2.1 to 4.5)	4.5 (3.1 to 6.0)	<.001
32-Question Inflammatory Bowel Disease Questionnaire score[n]	42.6 (39.7 to 45.6)	24.3 (20.2 to 28.5)	18.3 (13.4 to 23.3)	<.001
≥1 Ulcerative colitis–related hospitalization	5 (0.8) [0.1 to 1.4]	18 (5.5) [3.1 to 8.0]	−4.8 (−7.3 to −2.2)	<.001
No nocturnal bowel movements[k]	437 (67.3) [63.7 to 70.9]	140 (43.1) [37.7 to 48.5]	24.2 (17.9 to 30.5)	<.001
No tenesmus[k]	317 (48.7) [44.9 to 52.6]	98 (30.2) [25.2 to 35.1]	18.6 (12.4 to 24.8)	<.001
Fecal incontinence score, mean change (95% CI)[o]	−3.8 (−4.3 to −3.4)	−2.2 (−2.9 to −1.6)	−1.6 (−2.4 to −0.9)	<.001
Score for interrupted sleep due to ulcerative colitis symptoms, mean change (95% CI)[p]	−2.5 (−2.7 to −2.3)	−1.5 (−1.8 to −1.2)	−1.0 (−1.3 to −0.6)	<.001

Table 3. Primary and Key Secondary Outcomes in the Maintenance Trial

	No. (%) [97.5% CI][a]						
	Risankizumab administered subcutaneously			Risankizumab (180 mg) vs placebo		Risankizumab (360 mg) vs placebo	
	180 mg (n = 179)	360 mg (n = 186)	Placebo administered subcutaneously (n = 183)	Adjusted between-group difference, % (97.5% CI)[b]	P value[c]	Adjusted between-group difference, % (97.5% CI)[b]	P value[c]
Primary outcome							
Clinical remission (determined using the adapted Mayo score)[d,e]	72 (40.2) [31.9 to 48.4]	70 (37.6) [29.7 to 45.6]	46 (25.1) [17.9 to 32.3]	16.3 (6.1 to 26.6)	<.001	14.2 (4.0 to 24.5)	.002
Secondary outcomes							
Clinical response (determined using the adapted Mayo score)[d,f]	122 (68.2) [60.4 to 76.0]	116 (62.3) [54.4 to 70.3]	95 (51.9) [43.6 to 60.2]	17.1 (6.2 to 28.0)	<.001	11.5 (0.3 to 22.6)	.02
Improvement							
Endoscopic[g]	91 (50.8) [42.4 to 59.2]	90 (48.3) [40.1 to 56.5]	58 (31.7) [24.0 to 39.4]	20.1 (9.2 to 30.9)	<.001	17.4 (6.6 to 28.3)	<.001
Histological, endoscopic, and mucosal[h]	77 (42.8) [34.5 to 51.1]	79 (42.2) [34.1 to 50.4]	43 (23.5) [16.5 to 30.5]	20.2 (9.9 to 30.5)	<.001	19.8 (9.5 to 30.0)	<.001
Endoscopic remission[i]	41 (23.2) [16.1 to 30.3]	45 (24.3) [17.3 to 31.4]	27 (14.8) [8.9 to 20.6]	9.5 (0.8 to 18.2)	.01	9.8 (0.9 to 18.2)	.01
No bowel urgency[j]	96 (53.6) [45.3 to 62.0]	92 (49.4) [41.2 to 57.6]	57 (31.1) [23.5 to 38.8]	22.6 (11.8 to 33.5)	<.001	18.4 (7.4 to 29.3)	<.001
No abdominal pain[j]	84 (46.9) [38.6 to 55.3]	70 (37.8) [29.8 to 45.8]	54 (29.5) [22.0 to 37.1]	17.0 (6.0 to 28.0)	<.001	8.2 (−2.6 to 19.0)	.09
Histological, endoscopic, and mucosal remission[k]	23 (12.9) [7.3 to 18.6]	29 (15.6) [9.7 to 21.6]	18 (9.8) [4.9 to 14.8]	4.0 (−1.1 to 11.2)	.21	6.1 (−1.2 to 13.4)	.06
Mean change from induction baseline (95% CI)							
13-Item Functional Assessment of Chronic Illness Therapy-Fatigue scale score[l]	10.9 (8.5 to 13.4)	10.3 (7.8 to 12.8)	7.0 (4.6 to 9.5)	3.9 (0.8 to 7.0)	.005	3.3 (0.2 to 6.3)	.02
32-Question Inflammatory Bowel Disease Questionnaire score[m]	52.6 (43.8 to 61.3)	50.3 (41.0 to 59.5)	35.0 (26.0 to 44.1)	17.5 (6.6 to 28.4)	<.001	15.2 (3.7 to 26.8)	.003
≥1 Ulcerative colitis–related hospitalization, patients/100 person-years (97.5% CI)	0.6 (0 to 1.9)	1.2 (0 to 3.1)	3.1 (0 to 6.1)	−2.5 (−5.8 to 0.8)	.09	−1.8 (−5.5 to 1.8)	.25
No nocturnal bowel movement[j]	75 (41.9) [33.6 to 50.2]	81 (43.5) [35.3 to 51.6]	55 (30.1) [22.5 to 37.7]	12.0 (2.0 to 21.9)	.007	14.8 (4.8 to 24.7)	<.001
No tenesmus[j]	66 (36.9) [28.8 to 45.0]	68 (36.8) [28.8 to 44.8]	43 (23.5) [16.5 to 30.5]	13.1 (3.4 to 22.9)	.003	14.4 (4.5 to 24.3)	.001
Mean change from induction baseline (97.5% CI)							
Fecal incontinence score[n]	−3.4 (−4.0 to −2.0)	−2.9 (−4.5 to −1.3)	−2.8 (−4.4 to −1.1)	−0.7 (−2.8 to 1.5)	.48	−0.1 (−2.4 to 2.2)	.92
Score for interrupted sleep due to ulcerative colitis symptoms[o]	−2.6 (−3.2 to −1.9)	−2.5 (−3.1 to −1.9)	−1.8 (−2.4 to −1.2)	−0.8 (−1.7 to 0.07)	.04	−0.7 (−1.5 to 0.1)	.06
Clinical remission							
Sustained remission, No./total (%) [97.5% CI][p]	31/44 (70.2) [54.7 to 85.8]	20/40 (50.0) [32.3 to 67.7]	21/53 (39.6) [24.6 to 54.7]	29.2 (7.4 to 51.0)	.003	12.5 (−10.5 to 35.6)	.22
Corticosteroid-free[q]	71 (39.6) [31.4 to 47.8]	69 (37.1) [29.2 to 45.0]	46 (25.1) [17.9 to 32.3]	15.8 (5.6 to 26.0)	<.001	13.7 (3.5 to 24.0)	.003
Sustained endoscopic remission, No./total (%) [97.5% CI][r]	45/61 (73.8) [60.9 to 86.3]	37/68 (54.1) [40.5 to 67.7]	37/78 (47.4) [34.8 to 60.1]	23.9 (6.4 to 41.4)	.002	4.8 (−13.7 to 23.2)	.56