JAMA

hospital pharmacy

期刊報告

藥品諮詢組

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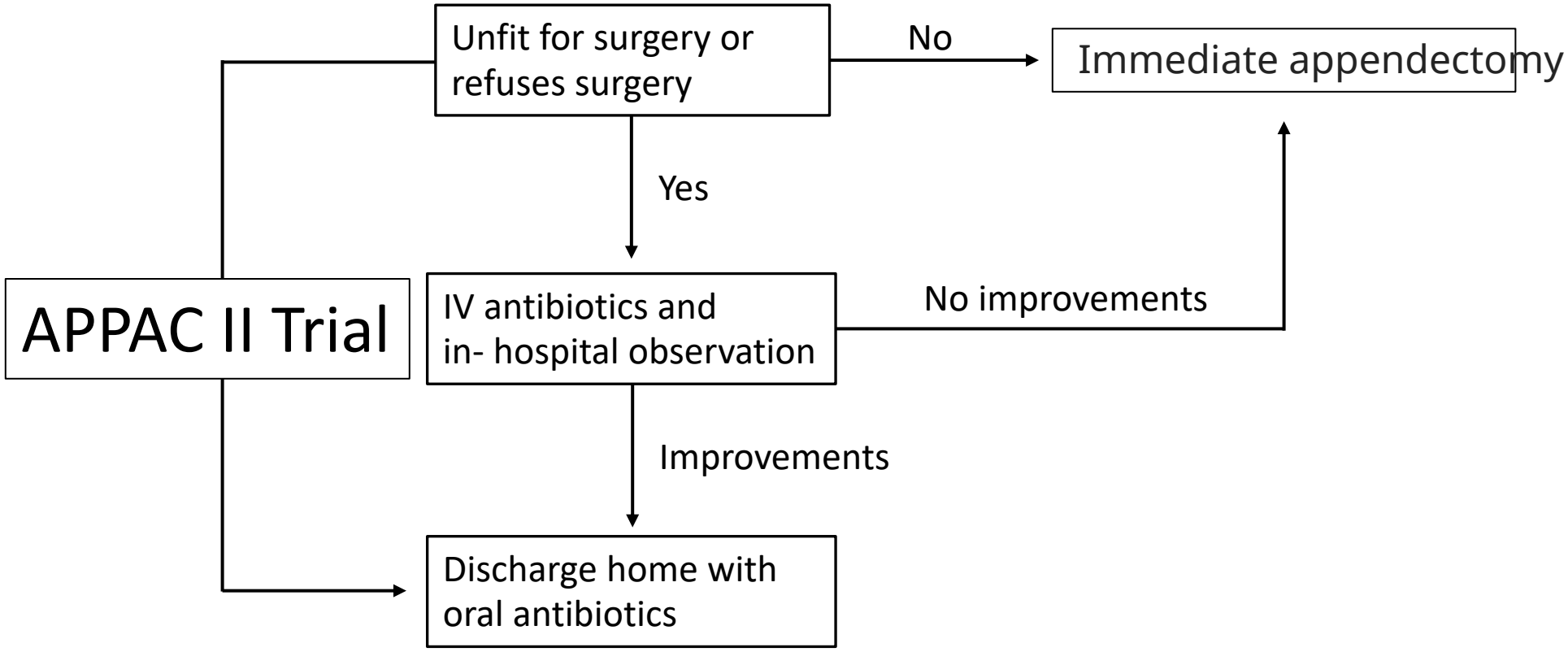
Effect of Oral Moxifloxacin vs Intravenous Ertapenem Plus Oral Levofloxacin for Treatment of Uncomplicated Acute Appendicitis

APPAC II

口服抗生素用於治療
uncomplicated acute appendicitis
是否不劣於先IV後轉口服抗生素

Treatment of uncomplicated acute appendicitis



Effect of Oral Moxifloxacin vs Intravenous Ertapenem Plus Oral Levofloxacin for Treatment of Uncomplicated Acute Appendicitis

Inclusion criteria

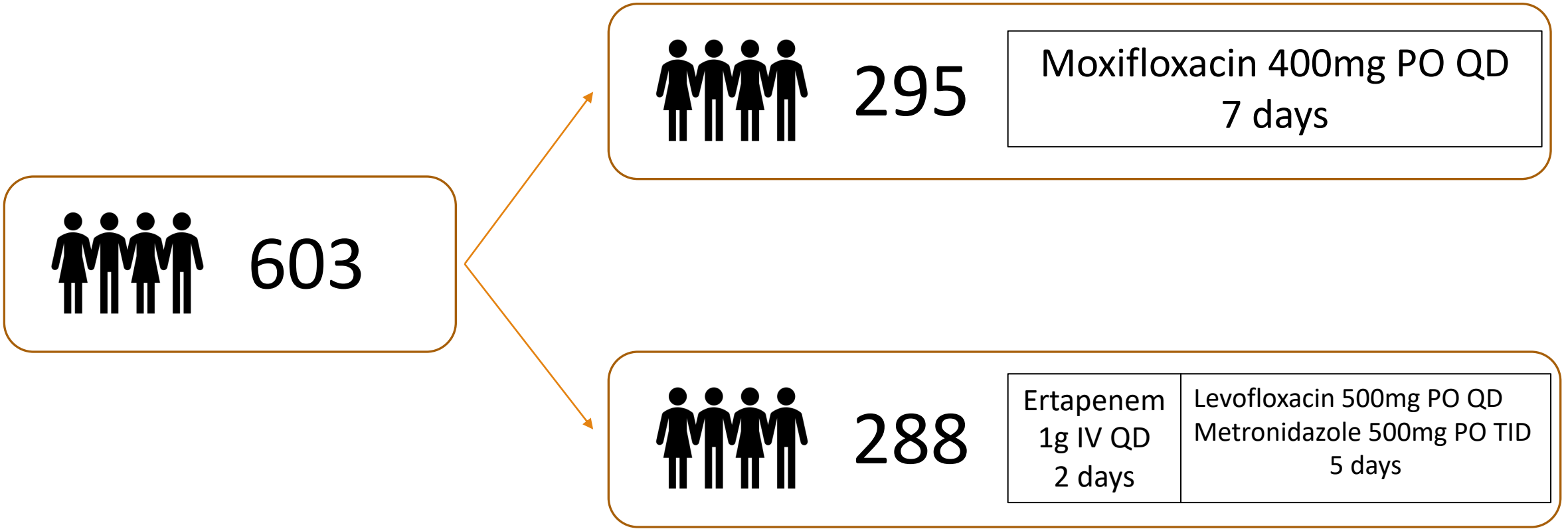
- 18-60 years
- Uncomplicated acute appendicitis confirmed by CT imaging
- Absence of the criteria of complicated appendicitis

Exclusion criteria

- Pregnancy or lactation
- Allergy to contrast media or iodine
- Allergy or contraindication to antibiotic therapy
- Type 2 DM and use of metformin
- Severe systemic illness

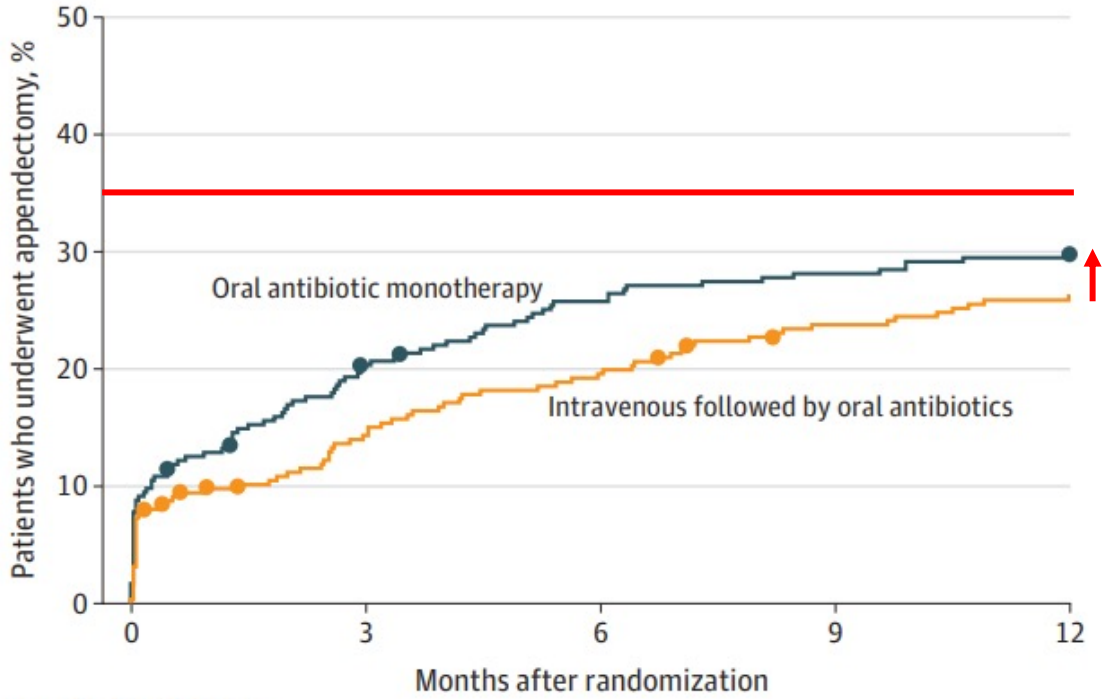
- Randomized
- Open-label
- Noninferiority
- Multi center
- Follow-up 1 year
- ITT analysis

Randomization and Interventions



Characteristic	Oral antibiotic monotherapy group (n = 301)	Intravenous followed by oral antibiotics group (n = 298)
Sex, No. (%)		
Women	137 (45.5)	126 (42.3)
Men	164 (54.5)	172 (57.7)
Age, median (IQR), y	34 (26-45)	33 (26-43)
Visual analog scale score for pain on admission, mean (SD)[b]	5.2 (2.3)	5.3 (2.4)
Body temperature, mean (SD), °C	37.2 (0.6)	37.2 (0.6)
Leukocyte count, median (IQR), ×10³/L[c]	12.5 (9.4-14.9)	12.2 (9.1-14.9)
C-reactive protein, median (IQR), mg/L[c]	29.9 (11.0-61.0)	34.0 (13.0-62.6)
BMI, median (IQR)	26.8 (24.2-30.1)	26.4 (23.6-30.2)
Appendiceal diameter	10.9 (2.6)	10.7 (2.4)
Duration of symptoms on admission, median (IQR), h	18.0 (10.0-30.0)	22.0 (12.0-30.0)

Result-Primary



No. of patients at risk

Oral antibiotic monotherapy				
295	235	219	212	207
Intravenous followed by oral antibiotics				
286	245	230	218	211

均有達成預設Treatment success標準

ARI: 3.6%

1-sided 95% CI: 9.7% (大於預設6%非劣性標準)

P: 0.26 (無統計上差異)

Outcome	Oral antibiotic monotherapy group (n = 295)	Intravenous followed by oral antibiotics group (n = 288)	Absolute mean difference (95% CI)	*P* value
Primary				
Treatment success at 1 year, %[a]	70.2	73.8 (n = 286)	−3.6% (1-sided 95% CI, −9.7% to ∞)	.26[b]

Result-Secondary

Outcome	Oral antibiotic monotherapy group (n = 295)	Intravenous followed by oral antibiotics group (n = 288)	Absolute mean difference (95% CI)	*P* value
Secondary				
Length of primary hospital stay, median (IQR), h	28.9 (23.0 to 41.9)	29.9 (23.3 to 43.2)	−0.77 (−3.9 to 2.4)	.38
Discharge	1.0 (0.0 to 2.0) [n = 265]	1.0 (0.0 to 2.0) [n = 263]	NA[d]	.91
1 wk	0.0 (0.0 to 0.0) [n = 265]	0.0 (0.0 to 0.5) [n = 252]	NA[d]	.84
2 mo	0.0 (0.0 to 0.0) [n = 262]	0.0 (0.0 to 0.0) [n = 248]	NA[d]	.38
Length of sick leave, median (IQR), d	7.0 (3.0 to 8.0)	7.0 (3.0 to 9.0)	0 (−0.70 to 0.70)	.42

No statistically significant difference

Result-Adverse Events

Adverse event	No.	
	Oral antibiotic monotherapy group (n = 295)	Intravenous followed by oral antibiotics group (n = 288)
Related to antibiotic treatment[a]	6	14
Skin eczema	3	3
Other miscellaneous symptoms related to antibiotic treatment		
Nausea	23	40
Diarrhea	11	36
Metallic taste sensation	1	23
Patients with at least 1 adverse event, No./total No. (%) [95% CI][c]	14/295 (4.8) [2.3-7.2]	21/286 (7.3) [4.3-10.4]

Conclusion

Oral antibiotic group		
Efficacy	V	1 year treatment success rate: 70.2%
Adverse event	V	Mostly the same, rate of nausea and diarrhea are lower than IV group
Noninferiority	X	95 % CI cross the preset 6% noninferiority margin
Limitation	V	• some patients incorrectly enrolled (n=4) or exclude (n=136) • margin for clinical importance of 6% were set somewhat arbitrarily

- Despite failed to demonstrate noninferiority but oral regiment can avoid hospitalization for the 70.2% of patients with acute appendicitis.

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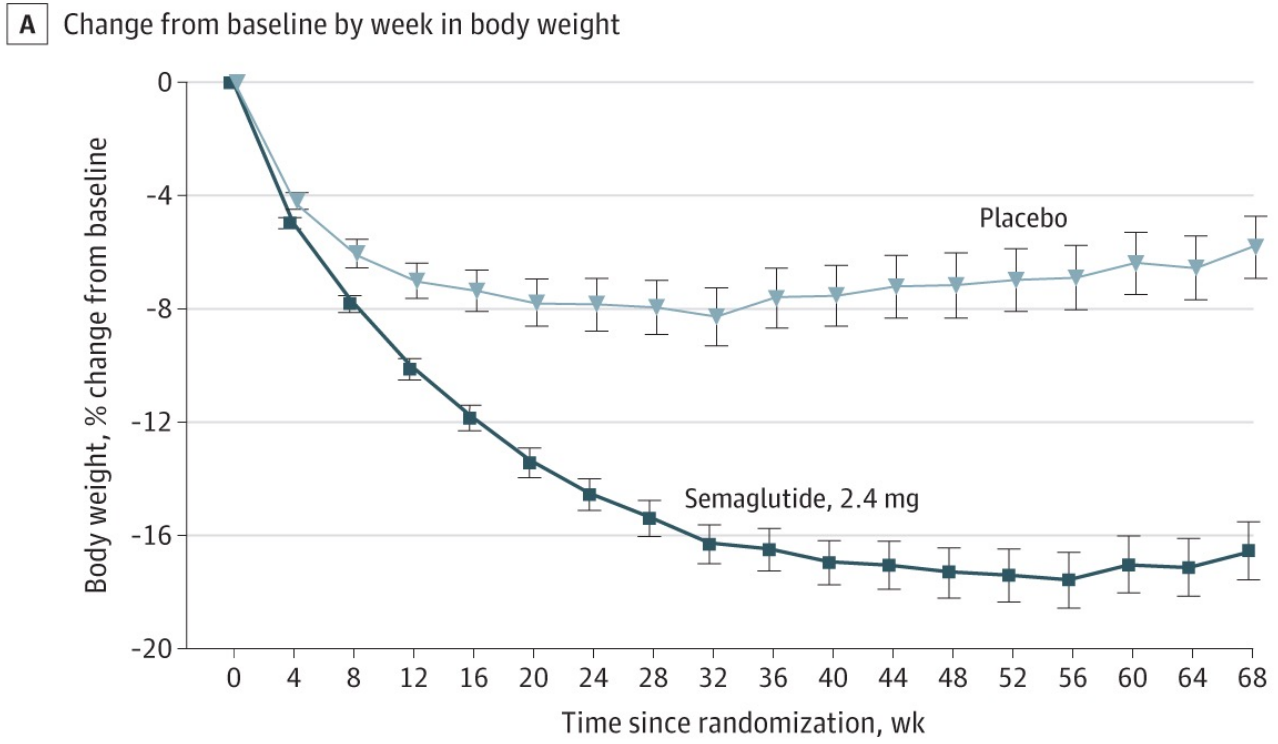
Effect of Continued Weekly Subcutaneous Semaglutide vs Placebo on Weight Loss Maintenance in Adults With Overweight or Obesity

STEP 4

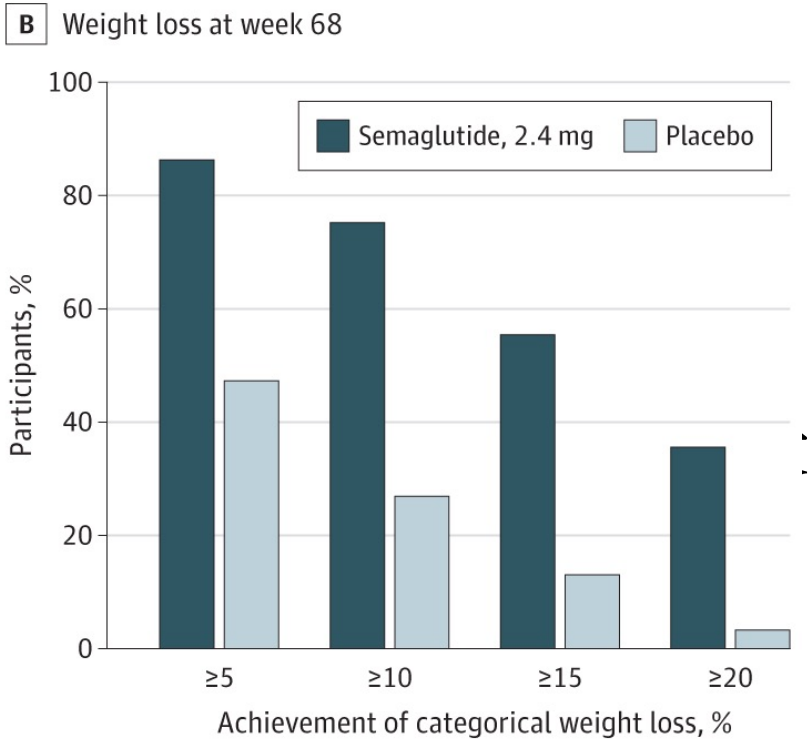
持續使用semaglutide對於體重控制的效果

STEP 3



No. of participants

Semaglutide, 2.4 mg	407	398	396	385	389	385	370	380	363	373	364	364	356	367	343	365	346	373
Placebo	204	200	197	190	194	194	185	189	180	189	180	184	172	183	170	180	166	189



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Effect of Continued Weekly Subcutaneous Semaglutide vs Placebo on Weight Loss Maintenance in Adults With Overweight or Obesity

STEP 4

持續使用semaglutide 對於體重控制的效果

Effect of Continued Weekly Subcutaneous Semaglutide vs Placebo on Weight Loss Maintenance in Adults With Overweight or Obesity

Inclusion criteria

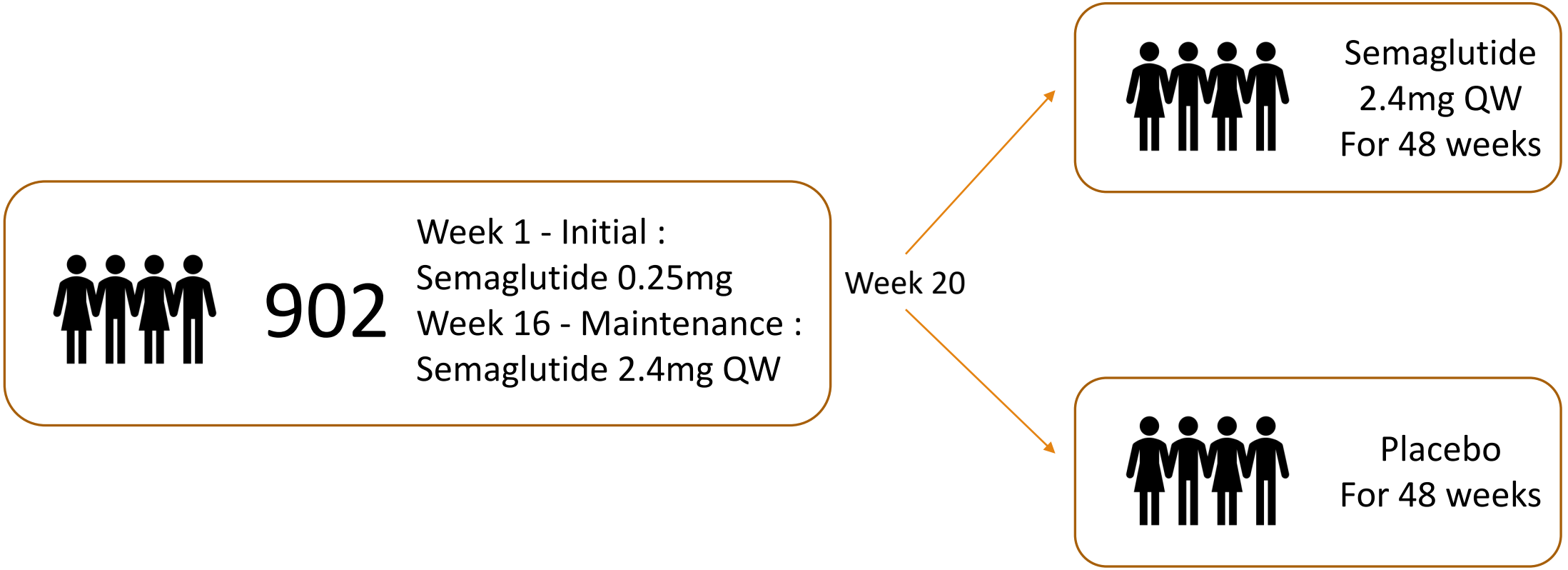
- ≥18 years
- At least 1 self-reported unsuccessful dietary effort to lose weight (BMI>30)
- At least 1 treated or untreated weight-related comorbidity (BMI>27)

Exclusion criteria

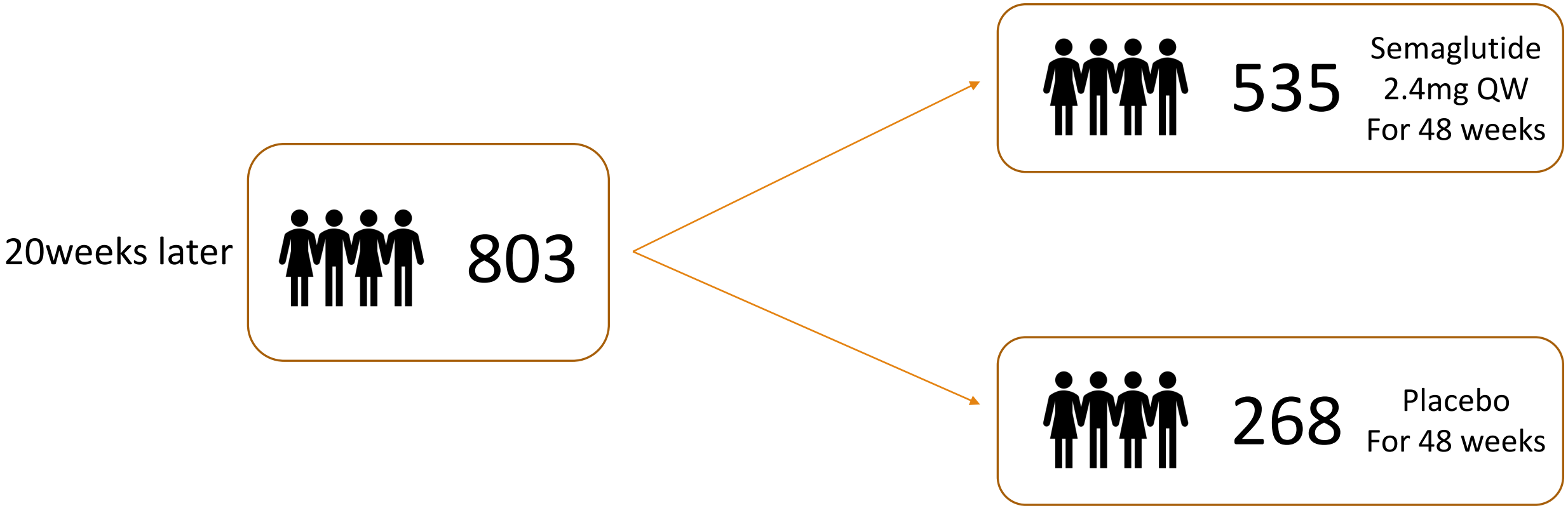
- HbA_{1c} > 6.5% (Type 2 DM)
- Self-reported change in body weight of more than 5 kg within 90 days

- Randomized
- Double-blind
- Phase IIIa
- International
- Multi center
- 68 weeks
- ITT analysis

Randomization and Interventions



Randomization and Interventions



Demographics and Clinical Characteristics

Table 1. Demographics and Clinical Characteristics at Week 0 and Week 20 (Full Analysis Set)

Characteristics	Week 0 (start of run-in period with semaglutide treatment) (n = 803)	Change during run-in period[a]	Week 20 (randomization)	
			Continued semaglutide, 2.4 mg/wk (n = 535)	Switched to placebo (n = 268)
Age, mean (SD), y	46 (12)		47 (12)	46 (12)
Sex, No. (%)				
Female	634 (79.0)		429 (80.2)	205 (76.5)
Male	169 (21.0)		106 (19.8)	63 (23.5)
Race, No. (%)[b]				
White	672 (83.7)		446 (83.4)	226 (84.3)
Black or African American	104 (13.0)		69 (12.9)	35 (13.1)
Asian	19 (2.4)		15 (2.8)	4 (1.5)
Other	8 (1.0)		5 (0.9)	3 (1.1)
Hispanic or Latino ethnicity, No. (%)	63 (7.8)		42 (7.9)	21 (7.8)
Body weight, mean (SD), kg	107.2 (22.7)	−11.1 (4.9)	96.5 (22.5)	95.4 (22.7)
Change, mean (SD), %		−10.6 (4.7)		
Body mass index[c]				
Mean (SD)	38.4 (6.9)	−4.0 (1.7)	34.5 (6.9)	34.1 (7.1)
No. (%)				
<25	0		7 (1.3)	9 (3.4)
≥25 to <30	22 (2.7)		153 (28.6)	69 (25.7)
≥30 to <35	274 (34.1)		166 (31.0)	97 (36.2)
≥35 to <40	249 (31.0)		116 (21.7)	52 (19.4)
≥40	258 (32.1)		93 (17.4)	41 (15.3)
Waist circumference, mean (SD), cm	115.3 (15.5)	−10.1 (6.2)	105.5 (15.9)	104.7 (16.9)
Blood pressure, mean (SD), mm Hg				
Systolic	127 (14)	−5.7 (13.6)	121 (13)	121 (13)
Diastolic	81 (10)	−3.0 (8.8)	78 (9)	78 (9)
Hemoglobin A_{1c}, mean (SD), %	5.7 (0.3)	−0.4 (0.2)[d]	5.4 (0.3)	5.4 (0.3)
Fasting plasma glucose, mean (SD), mg/dL	97.0 (10.7)	−9.5 (9.9)	87.9 (7.7)	86.9 (7.6)
Fasting lipids, median (IQR), mg/dL[e,f]				
Total cholesterol	194.6 (170.3-218.1) [n = 798]	0.9 (0.8-1.0)[g]	177.2 (152.9-201.9)	177.6 (156.0-198.8)
HDL-C	50.2 (42.1-59.1) [n = 798]	0.9 (0.8-1.0)[g]	44.4 (37.8-51.7)	44.0 (36.5-51.0)
LDL-C	116.6 (97.3-138.6) [n = 798]	1.0 (0.8-1.1)[g]	110.4 (91.1-130.9)	112.5 (93.6-130.9)
VLDL-C	22.8 (17.4-32.0) [n = 798]	0.8 (0.7-1.0)[g]	18.5 (14.3-24.7)	17.8 (13.5-24.7)
Free fatty acids	13.0 (9.0-17.8) [n = 789]	1.0 (0.7-1.4)[g]	12.5 (9.0-18.0) [n = 534]	12.5 (8.5-17.9)
Triglycerides	117.5 (88.1-164.7) [n = 798]	0.8 (0.7-1.0)[g]	95.2 (73.9-125.5)	90.8 (69.4-126.4)
SF-36 physical functioning score, mean (SD)[e,h]	51.7 (6.4) [n = 801]	2.2 (5.1)	53.8 (5.7) [n = 534]	54.1 (5.0)
Pulse, mean (SD), /min[i]	71 (10)	4.8 (9.3)	76 (9)	76 (9)
eGFR, median (IQR), mL/min/1.73 m^2[f,i,j]	100.5 (87.7-110.9)	1.0 (0.9-1.0)[g]	94.2 (81.3-106.6)	95.9 (83.5-108.1)
Comorbidities at screening, No. (%)				
Dyslipidemia	288 (35.9)		189 (35.3)	99 (36.9)
Hypertension	298 (37.1)		199 (37.2)	99 (36.9)
Knee osteoarthritis	99 (12.3)		72 (13.5)	27 (10.1)
Obstructive sleep apnea	94 (11.7)		61 (11.4)	33 (12.3)
Asthma/COPD	92 (11.5)		57 (10.7)	35 (13.1)
Nonalcoholic fatty liver disease	55 (6.8)		37 (6.9)	18 (6.7)
Polycystic ovary syndrome	25 (3.9)		15 (3.5)	10 (4.9)
Coronary artery disease	7 (0.9)		4 (0.7)	3 (1.1)

Demographics and Clinical Characteristics

BMI> 30: 97.2%

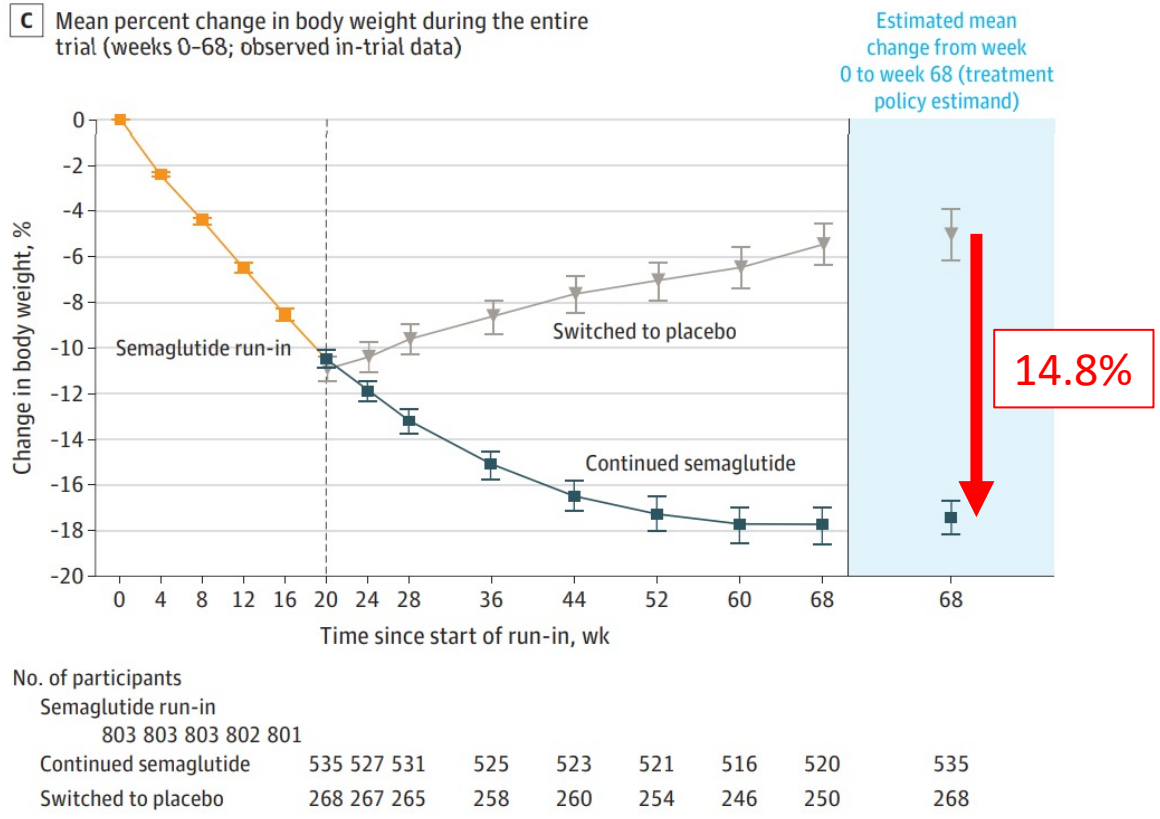
HTN: 37.1%

Dyslipidemia: 35.9%

Table 1. Demographics and Clinical Characteristics at Week 0 and Week 20 (Full Analysis Set) (continued)

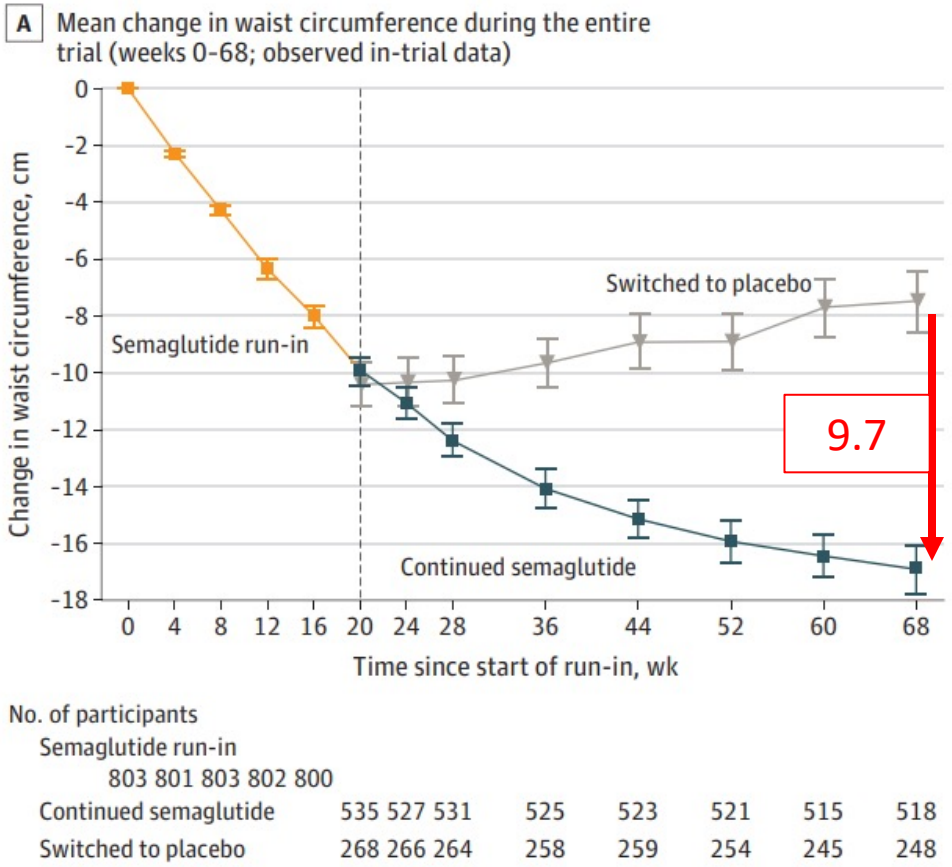
Characteristics	Week 0 (start of run-in period with semaglutide treatment) (n = 803)	Change during run-in period[a]	Week 20 (randomization)	
			Continued semaglutide, 2.4 mg/wk (n = 535)	Switched to placebo (n = 268)
Comorbidities at screening, No. (%)[i,k]				
0	214 (26.7)		144 (26.9)	70 (26.1)
1	238 (29.6)		160 (29.9)	78 (29.1)
2	171 (21.3)		103 (19.3)	68 (25.4)
3	111 (13.8)		77 (14.4)	34 (12.7)
4	53 (6.6)		38 (7.1)	15 (5.6)
≥5	16 (2.0)		13 (2.4)	3 (1.1)

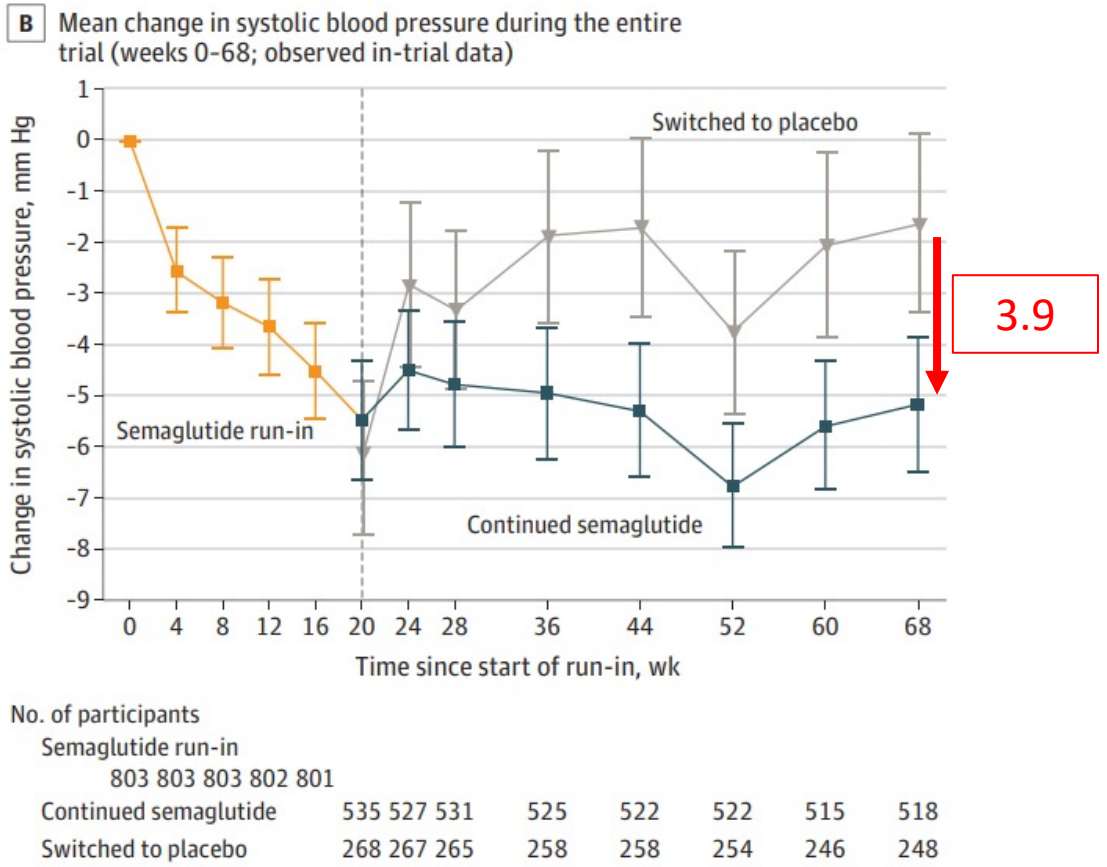
Result – Primary



	Body weight change
Switched to placebo	+ 6.9%
Continued semaglutide	- 7.9%
P value < 0.01	

Result – Secondary





Result-Adverse Events

Table 3. Adverse Event and Tolerability Profile During the Randomized Period (Weeks 20-68; Safety Analysis Set)

Adverse events	Continued semaglutide, 2.4 mg/wk (n = 535)			Switched to placebo (n = 268)		
	No. (%) of participants	No. of events	Events per 100 patient-years[a]	No. (%) of participants	No. of events	Events per 100 patient-years[a]
Any adverse event	435 (81.3)	1885	346.3	201 (75.0)	779	292.8
Serious adverse events	41 (7.7)	51	9.4	15 (5.6)	19	7.1
Discontinuation of trial product due to adverse events[b]	13 (2.4)			6 (2.2)		
Fatal events[c,d]	1 (0.2)	1	0.2	1 (0.4)	2	0.7
Adverse events reported in ≥5% of participants[e]						
Diarrhea	77 (14.4)	114	20.9	19 (7.1)	26	9.8
Nausea	75 (14.0)	105	19.3	13 (4.9)	13	4.9
Constipation	62 (11.6)	75	13.8	17 (6.3)	19	7.1
Nasopharyngitis	58 (10.8)	77	14.1	39 (14.6)	54	20.3
Vomiting	55 (10.3)	88	16.2	8 (3.0)	13	4.9
Headache	41 (7.7)	48	8.8	10 (3.7)	10	3.8
Influenza	39 (7.3)	45	8.3	19 (7.1)	23	8.6
Abdominal pain	35 (6.5)	46	8.5	8 (3.0)	10	3.8
Back pain	28 (5.2)	32	5.9	18 (6.7)	19	7.1
Arthralgia	25 (4.7)	28	5.1	14 (5.2)	16	6.0
Safety areas of interest (MedDRA)[f]						
Gastrointestinal disorders	224 (41.9)	607	111.5	70 (26.1)	124	46.6
Psychiatric disorders	46 (8.6)	55	10.1	35 (13.1)	50	18.8
Cardiovascular disorders[c]	26 (4.9)	32	5.7	30 (11.2)	40	14.2
Allergic reactions	26 (4.9)	29	5.3	11 (4.1)	12	4.5
Gallbladder-related disorders	15 (2.8)	17	3.1	10 (3.7)	11	4.1
Injection site reactions	14 (2.6)	15	2.8	6 (2.2)	6	2.3
Hepatic disorders	11 (2.1)	12	2.2	4 (1.5)	4	1.5
Malignant neoplasms[c]	6 (1.1)	6	1.1	1 (0.4)	2	0.7
Hypoglycemia	3 (0.6)	3	0.6	3 (1.1)	3	1.1
Acute kidney failure	1 (0.2)	1	0.2	1 (0.4)	1	0.4
Acute pancreatitis	0			0		

	Semaglutide	Placebo
Diarrhea	14.4%	7.1%
Constipation	11.6%	6.3%
Nausea	14%	4.9%
Vomiting	10.3%	3%
Abdominal pain	6.5%	3%
Headache	7.7%	3.7%
GI disorders	41.9%	26.1%

Conclusion

Oral antibiotic group		
Efficacy	V	• Weight lost sustained and continued → -18% compared with baseline • Improvements in obesity related complications
Adverse event	V	• Similar to other GLP-1 agonists
Limitation	V	• Inflexibility, assessment to only participants tolerating the strict dose titration schedule → Effect size in clinical use is likely to be less

- This study supporting semaglutide use for long-term treatment of obesity.
- If tolerable to higher dose(2.4mg QW), smeaglutide exhibit best weight reduction compare to current approved pharmacotherapy.

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Effect of Postreinduction Therapy Consolidation With Blinatumomab vs Chemotherapy on Disease-Free Survival in Children, Adolescents, and YoungAdults With FirstRelapse of B-CellAcute Lymphoblastic Leukemia

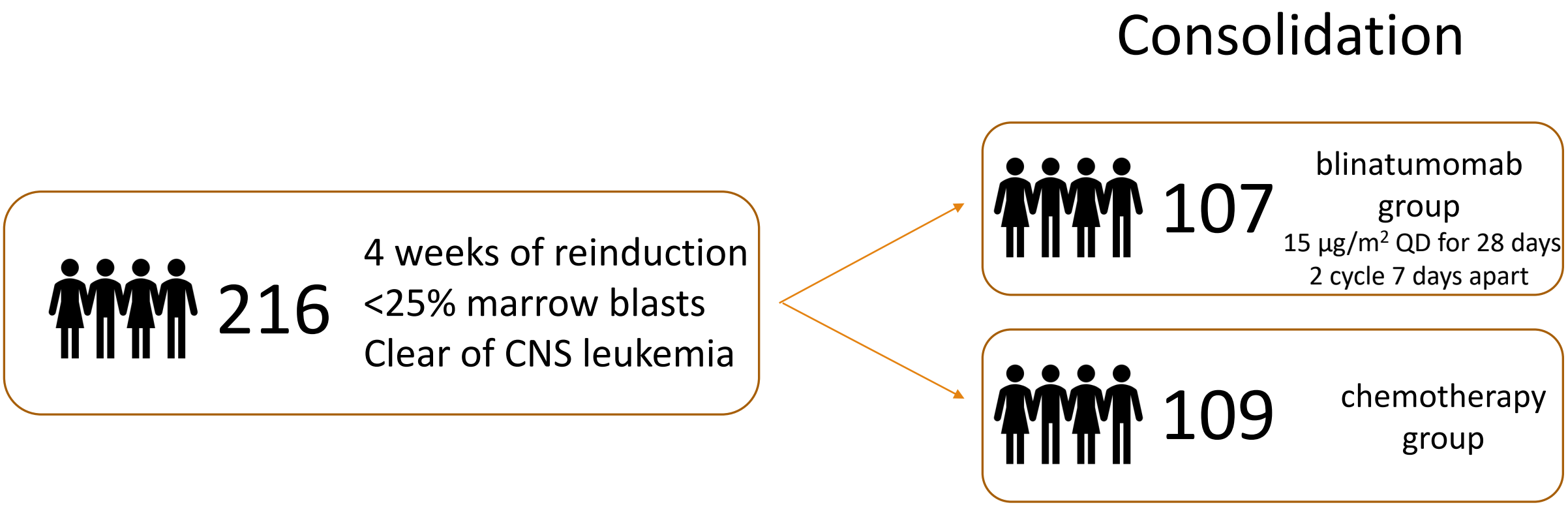
對於intermediate to high risk first relapse of B-ALL的病人使用Blinatumomab相較化療作為consolidation therapy是否能改善survival

Effect of Postreinduction Therapy Consolidation With Blinatumomab vs Chemotherapy on Disease-Free Survival in Children, Adolescents, and YoungAdults With FirstRelapse of B-CellAcute Lymphoblastic Leukemia

Inclusion criteria
• 1 to 30 years • B-ALL first relapse
Exclusion criteria
• Down syndrome • Philadelphia chromosome–positive ALL • Previous transplant • Previous blinatumomab treatment

- Randomized
- Phase IIIa
- International
- Multi center
- Early termination
- Median follow-up: 2.9 years
- ITT analysis

Randomization and Interventions

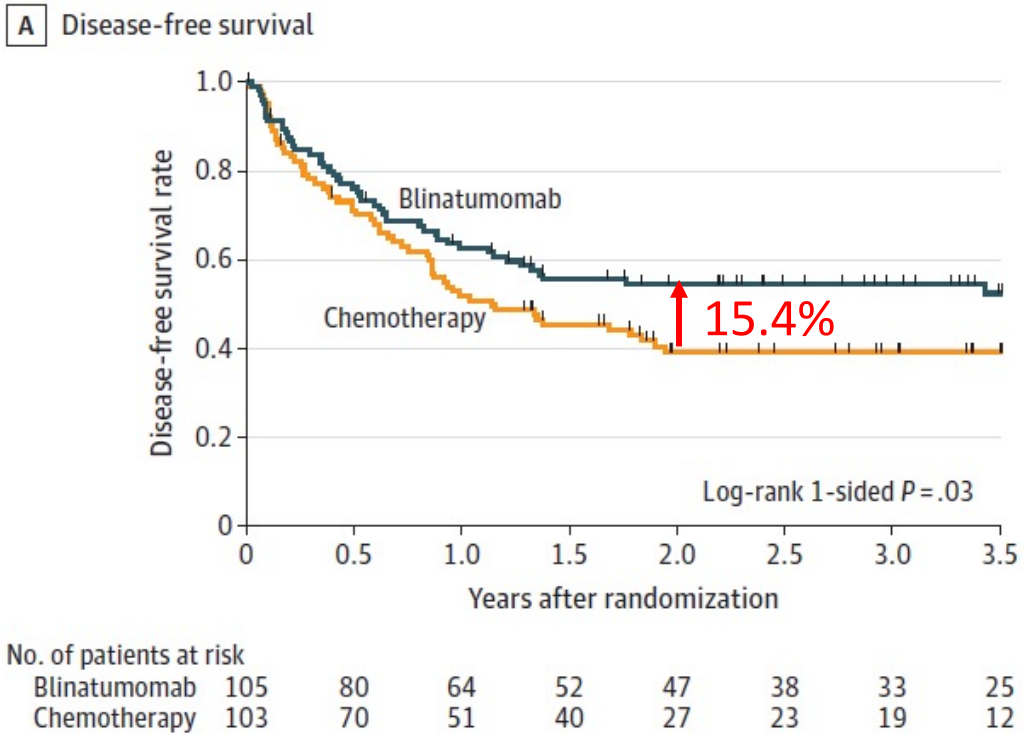


Demogra cteristics

Site of relapse		
Marrow (≥36 mo after diagnosis)	36 (34.3)	34 (33.0)
Marrow (18-36 mo after diagnosis)	41 (39.0)	41 (39.8)
MRD ≥0.1%, No.[b]	19	19

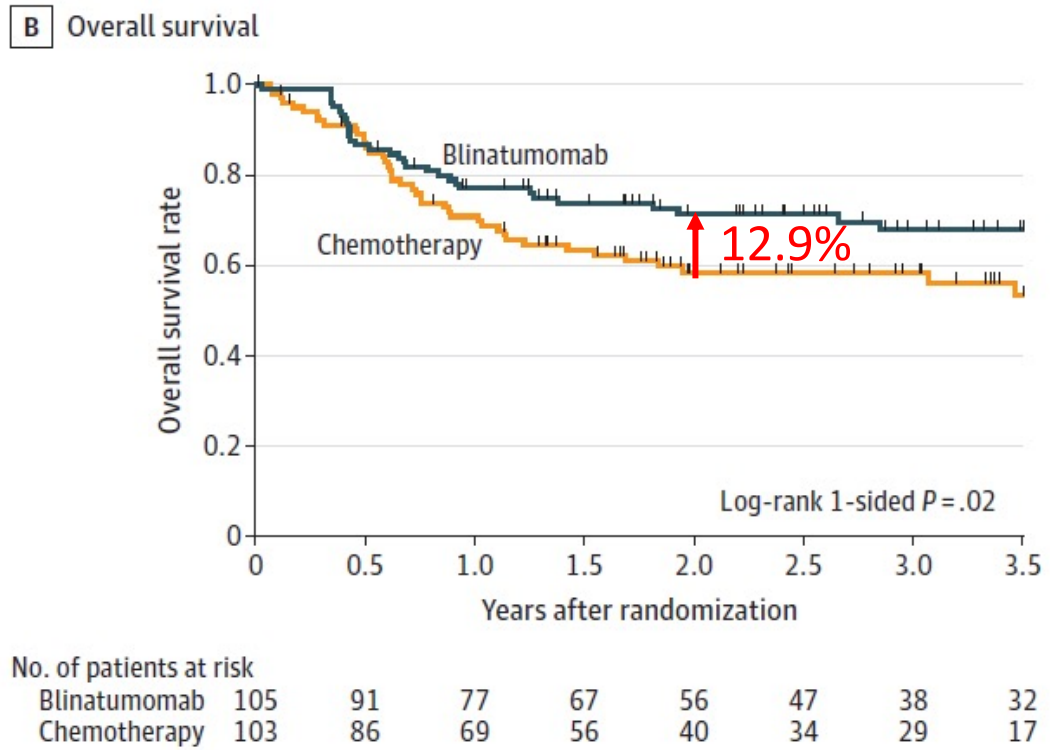
Characteristic	No. (%)	
	Blinatumomab (n = 105)	Chemotherapy (n = 103)
Cytogenetic group[e]		
Favorable	21 (23.3)	16 (17.6)
ETV6-RUNX1, No.	12	8
Hyperdiploid with +4, +10, No.	9	8
Unfavorable	7 (7.8)	10 (11)
KMT2A-rearranged, No.	7	9
Hypodiploid, No.	0	1
Other	62 (68.9)	65 (71.4)
Unknown, No.	15	12
Intermediate risk	36 (34.3)	34 (33.0)

Result – Primary



2-year disease-free survival	
Blinatumomab	54.4%
Chemotherapy	39.0%
ARR : 15.4% HR : 0.7 95% CI : 0.47 – 1.03 1-sided P Value : 0.03	Statistically insignificant

Result – Secondary



2-year overall survival	
Blinatumomab	71.3%
Chemotherapy	58.4%
ARR : 12.9% HR : 0.62 95% CI : 0.39 – 0.98 1-sided P Value : 0.02	Statistically significant

Result – Exploratory

	No. (%)				
	Blinatumomab (n = 105)	Chemotherapy (n = 103)	Absolute difference (95% CI), %	Odds ratio (95% CI)[a]	*P* value[a]
Exploratory end points[d]					
Negative MRD at the end of reinduction	26 (25)	31 (30)	−5 (−17 to 7)	0.76 (0.4 to 1.5)[e]	.39
Negative MRD at the end of cycle 1	79 (75)	33 (32)	43 (31 to 55)	6.4 (3.4 to 12.4)[e]	<.001
Negative MRD at the end of cycle 2	69 (66)	33 (32)	34 (21 to 46)	4.1(2.2 to 7.6)[e]	<.001
Underwent hematopoietic stem cell transplant[f]	74 (70)	44 (43)	27 (15 to 41)	3.2 (1.7 to 5.9)	<.001

Result – Adverse Events

	No. (%)							
	Cycle 1				Cycle 2			
	Blinatumomab (n = 102)		Chemotherapy (n = 97)		Blinatumomab (n = 88)		Chemotherapy (n = 62)	
Adverse event	Any grade	Grade ≥3[a]	Any grade	Grade ≥3[a]	Any grade	Grade ≥3[a]	Any grade	Grade ≥3[a]
Patients with any adverse event	99 (97)	77 (76)	89 (92)	88 (91)	81 (92)	49 (56)	55 (89)	52 (84)
Anemia	77 (76)	15 (15)	63 (65)	51 (53)	39 (44)	4 (5)	36 (58)	35 (57)
White blood cell decreased	67 (66)	25 (25)	59 (61)	55 (57)	50 (57)	13 (15)	30 (48)	30 (48)
Alanine aminotransferase increased	65 (64)	12 (12)	62 (64)	38 (39)	37 (42)	6 (7)	27 (44)	8 (13)
Fever	54 (53)	6 (6)	24 (25)	5 (5)	20 (23)	2 (2)	20 (32)	6 (10)
Neutrophil count decreased	51 (50)	34 (33)	58 (60)	57 (59)	43 (49)	25 (28)	32 (52)	31 (50)
Aspartate aminotransferase increased	49 (48)	9 (9)	51 (53)	14 (14)	26 (30)	1 (1)	24 (39)	3 (5)
Hypoalbuminemia	47 (46)	0	43 (44)	6 (6)	18 (21)	0	23 (37)	1 (2)
Lymphocyte count decreased	43 (42)	37 (36)	32 (33)	30 (31)	33 (38)	18 (21)	16 (26)	15 (24)
Platelet count decreased	43 (42)	8 (8)	63 (65)	56 (58)	18 (21)	3 (3)	37 (60)	34 (55)
Hyperglycemia	32 (31)	2 (2)	24 (25)	6 (6)	31 (35)	2 (2)	19 (31)	8 (13)
Hypocalcemia	31 (30)	2 (2)	36 (37)	6 (6)	12 (14)	0	18 (29)	0
Hypokalemia	28 (28)	7 (7)	36 (37)	19 (20)	21 (24)	2 (2)	28 (45)	14 (23)
Hypophosphatemia	18 (18)	0	18 (19)	5 (5)	8 (9)	0	7 (11)	2 (3)
Hypotension	16 (16)	1 (1)	11 (11)	7 (7)	12 (14)	3 (3)	7 (11)	4 (7)
Blood bilirubin increased	15 (15)	2 (2)	31 (32)	7 (7)	4 (5)	0	16 (26)	2 (3)
Infection[b,c]	15 (15)	10 (10)	48 (49)	39 (40)	20 (23)	9 (10)	42 (68)	38 (61)
Vomiting	14 (14)	0	20 (21)	2 (2)	15 (17)	1 (1)	13 (21)	4 (7)
GGT increased	12 (12)	4 (4)	9 (9)	5 (5)	5 (6)	1 (1)	3 (5)	1 (2)
Anorexia	11 (11)	4 (5)	15 (16)	12 (12)	6 (7)	2 (2)	8 (13)	4 (7)
Febrile neutropenia[b]	6 (6)	5 (5)	43 (44)	43 (44)	0	0	28 (45)	28 (45)
Mucositis oral[b]	4 (4)	0	44 (45)	25 (26)	2 (2)	1 (1)	16 (26)	5 (8)
Sepsis[b]	1 (1)	1 (1)	13 (13)	13 (13)	2 (2)	2 (2)	14 (23)	14 (23)
Typhlitis	0	0	1 (1)	1 (1)	0	0	4 (7)	4 (7)

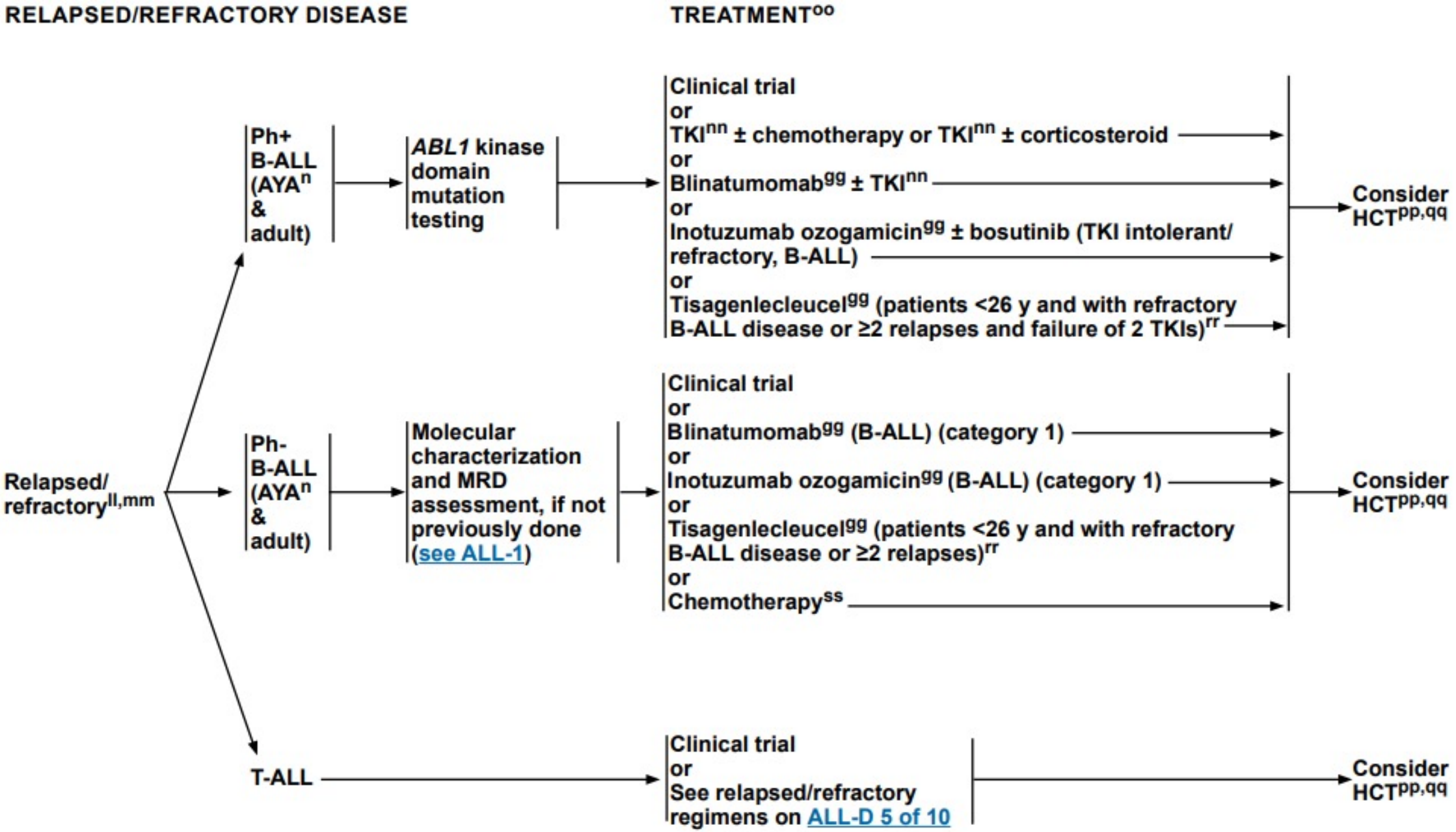
Cumulative grade ≥ 3 AE for cycle 1 and cycle 2

	Blinatumomab	Chemotherapy
Any AE	81.4%	92.8%
Lymphocyte count decreased	40.2%	34%
Infection	15%	65%
Febrile neutropenia	5%	58%
Mucositis	1%	28%
Sepsis	2%	27%

Conclusion

Blinatumomab group		
Efficacy	?	• Increase 2-year disease free survival 15.4%, HR: 0.7 ■ Statistically insignificant • Increase 2-year overall survival 12.9%, HR: 0.62 • Increase negative MRD rate(43%, 34%) and chance of HCT (27%)
Adverse event	V	• Mostly lower than chemotherapy group, especially in life-threatening complications
Limitation	V	• Early termination • Transplant procedures not fully standardized

- Using Blinatumomab as consolidation medication might increase patient outcome (disease free survival) and reduce adverse event.


RELAPSED/REFRACTORY DISEASE
TREATMENT[oo]
Relapsed/ refractory[ll,mm]
Ph+ B-ALL (AYA[n] & adult)
ABL1 kinase domain mutation testing
Clinical trial
or
TKI[nn] ± chemotherapy or TKI[nn] ± corticosteroid
or
Blinatumomab[gg] ± TKI[nn]
or
Inotuzumab ozogamicin[gg] ± bosutinib (TKI intolerant/ refractory, B-ALL)
or
Tisagenlecleucel[gg] (patients <26 y and with refractory B-ALL disease or ≥2 relapses and failure of 2 TKIs)[rr]
Consider HCT[pp,qq]
Ph- B-ALL (AYA[n] & adult)
Molecular characterization and MRD assessment, if not previously done (see ALL-1)
Clinical trial
or
Blinatumomab[gg] (B-ALL) (category 1)
or
Inotuzumab ozogamicin[gg] (B-ALL) (category 1)
or
Tisagenlecleucel[gg] (patients <26 y and with refractory B-ALL disease or ≥2 relapses)[rr]
or
Chemotherapy[ss]
Consider HCT[pp,qq]
T-ALL
Clinical trial
or
See relapsed/refractory regimens on ALL-D 5 of 10
Consider HCT[pp,qq]

JAMA

Effect of Half-Dose vs Stable-Dose Conventional Synthetic Disease-Modifying Antirheumatic Drugs on Disease Flares in Patients With Rheumatoid Arthritis in Remission

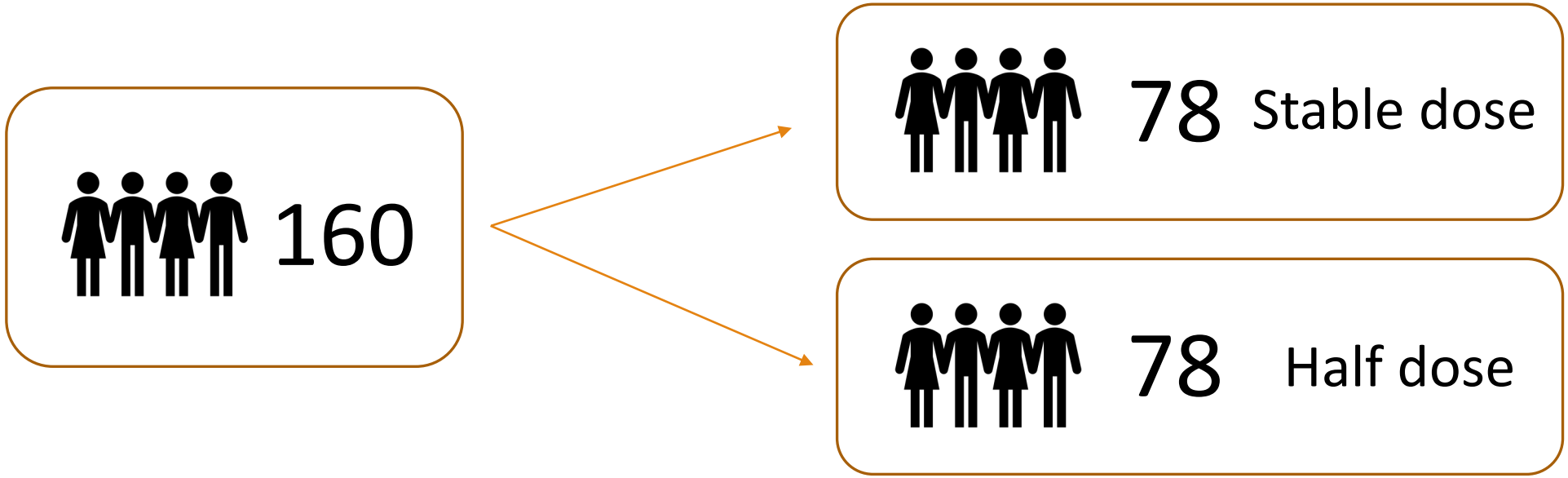
對於處於remission狀態的RA病患使用half-dose的csDMARD是否會增加flares的風險

Effect of Half-Dose vs Stable-Dose Conventional Synthetic Disease-Modifying Antirheumatic Drugs on Disease Flares in Patients With Rheumatoid Arthritis in Remission

Inclusion criteria
• 18 to 80 years • 2010 ACR or EULAR criteria RA • At least 12 months of remission status • Absence of any swollen joints, remission according to DAS
Exclusion criteria
• Change in csDMARD within 12 months • Use of biologic DMARD or JAK inhibitor • Oral glucocorticoid exceed equivalent to 5mg of prednisolone • Abnormal liver or kidney function

- Randomized
- Open label
- Noninferiority
- Multi center
- follow-up 12 months
- PP analysis

Randomization and Interventions



Demographics and Clinical Characteristics

Characteristic	Median (interquartile range) Half dose (n = 78)	Stable dose (n = 78)
Age, mean (SD), y	55.5 (12.0)	55.1 (11.8)
Sex, No. (%)		
Female	54 (69)	50 (64)
Male	24 (31)	28 (36)
Time since first swollen joint, y	3.2 (2.4-4.1)	3.4 (2.6-4.4)
Positive, No. (%)		
For anticitrullinated peptide antibodies	63 (81)	57 (73)
For rheumatoid factor	53 (68)	54 (69)
Body mass index[b]	25.7 (23.6-28.0)	25.7 (22.8-28.4)
Current smoker, No. (%)	13 (17)	14 (18)
Measures of disease activity		
Disease Activity Score, mean (SD)[c]	0.8 (0.3)	0.8 (0.4)
Simplified Disease Activity Index[d]	0.9 (0.3-2.1)	0.8 (0.5-1.6)
ACR/EULAR remission, No. (%)[e]	51 (65)	61 (78)
Swollen joint count, mean (SD)[f]	0	0
Tender joint count (Ritchie Articular Index)[g]	0 (0-0)	0 (0-0)
Erythrocyte sedimentation rate, mm/h (normal value <17 mm/h in women and <12 mm/h in men)[h]	7.0 (4.0-14.0)	7.0 (4.0-14.0)
C-reactive protein, mg/dL (normal value <0.4 mg/dL)[h]	0.2 (0.1-0.3)	0.2 (0.1-0.3)
Global assessment (0-10)[i]		
Patient's	3.5 (1.0-11.0)	3.5 (1.0-10.0)
Physician's	0 (0-3.0)	1.0 (0-4.0)
Functional outcomes		
PROMIS Physical Function, mean (SD)[j]	55.6 (7.5)	56.1 (7.4)
Visual analog scale (0-100 mm)[k]		
Fatigue	10.0 (2.0-30.0)	5.5 (1.0-24.0)
Joint pain	3.5 (1.0-10.0)	3.0 (1.0-9.0)
Radiographic joint damage		
Total van der Heijde-modified Sharp score[l]	4.5 (2.0-8.5)	5.0 (2.0-11.5)
van der Heijde-modified Sharp score		
Erosion	2.0 (1.0-3.5)	2.0 (1.0-4.5)
Sharp joint space narrowing	2.0 (0.5-6.0)	2.0 (0.5-8.0)
Ultrasound outcomes[m]		
Total power Doppler signal score	0 (0-0)	0 (0-0)
Total gray scale score	1.0 (0-3.0)	1.0 (0-2.0)
No power Doppler signal in any joint, No. (%)	72 (92)	72 (94)

Characteristic	Median (interquartile range) Half dose (n = 78)	Stable dose (n = 78)
Medication, No. (%)		
Methotrexate monotherapy		
By mouth	52 (67)	51 (65)
Subcutaneous	14 (18)	10 (13)
Methotrexate, sulfasalazine, and hydroxychloroquine	6 (8)	10 (13)
Other monotherapies or duotherapies	6 (8)	7 (9)
Dose in users, mean (SD)		
Methotrexate, mg/wk	19.5 (4.3)	19.0 (4.7)
Sulfasalazine, mg/d	1563 (623)	1769 (438)
Hydroxychlorochine, mg/d	378 (67)	400 (0)
Leflunomide, mg/d	20.0 (NC)	20.0 (NC)

Mean age: 55

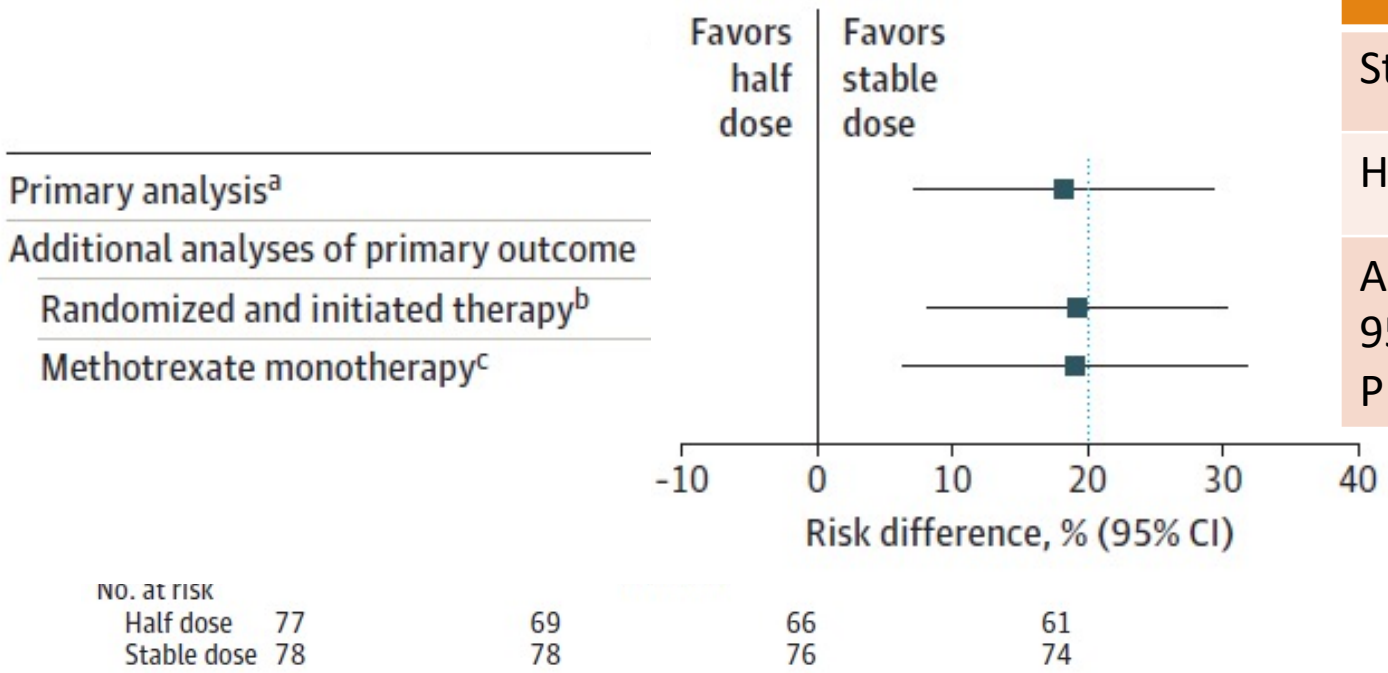
Female > Male

DAS: 0.8

ESR: 7.0

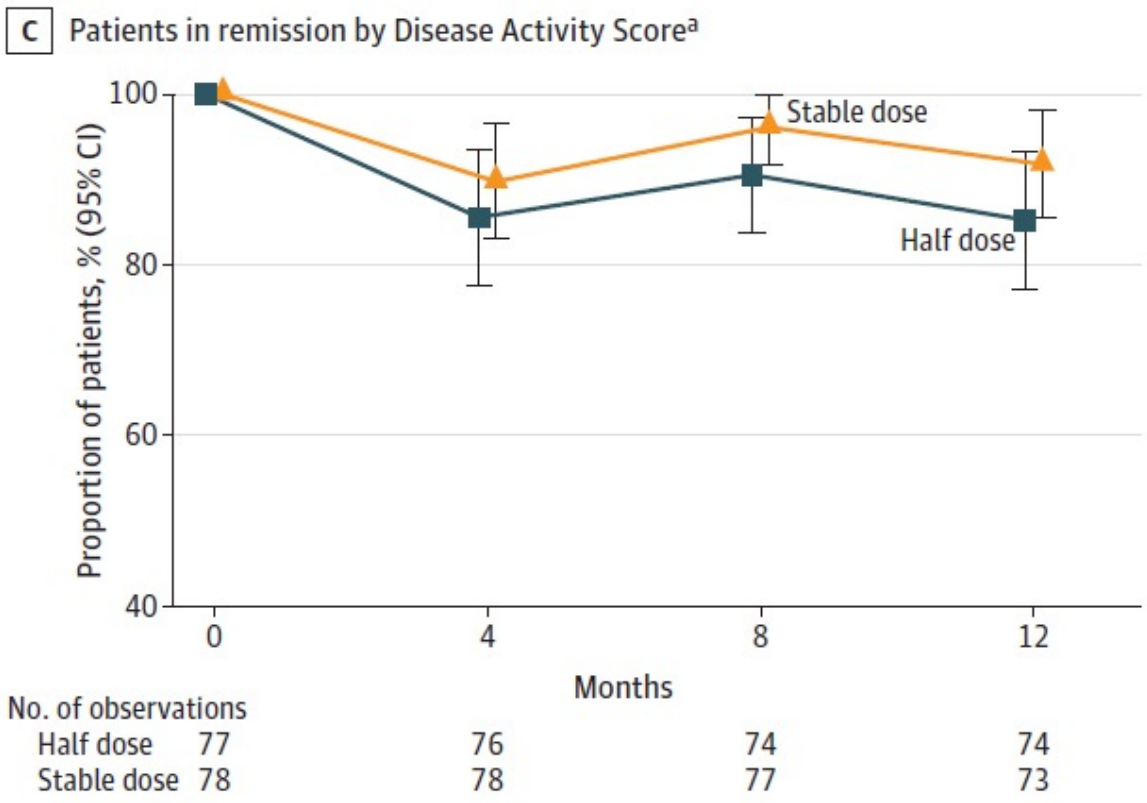
CRP: 0.2

Result – Primary



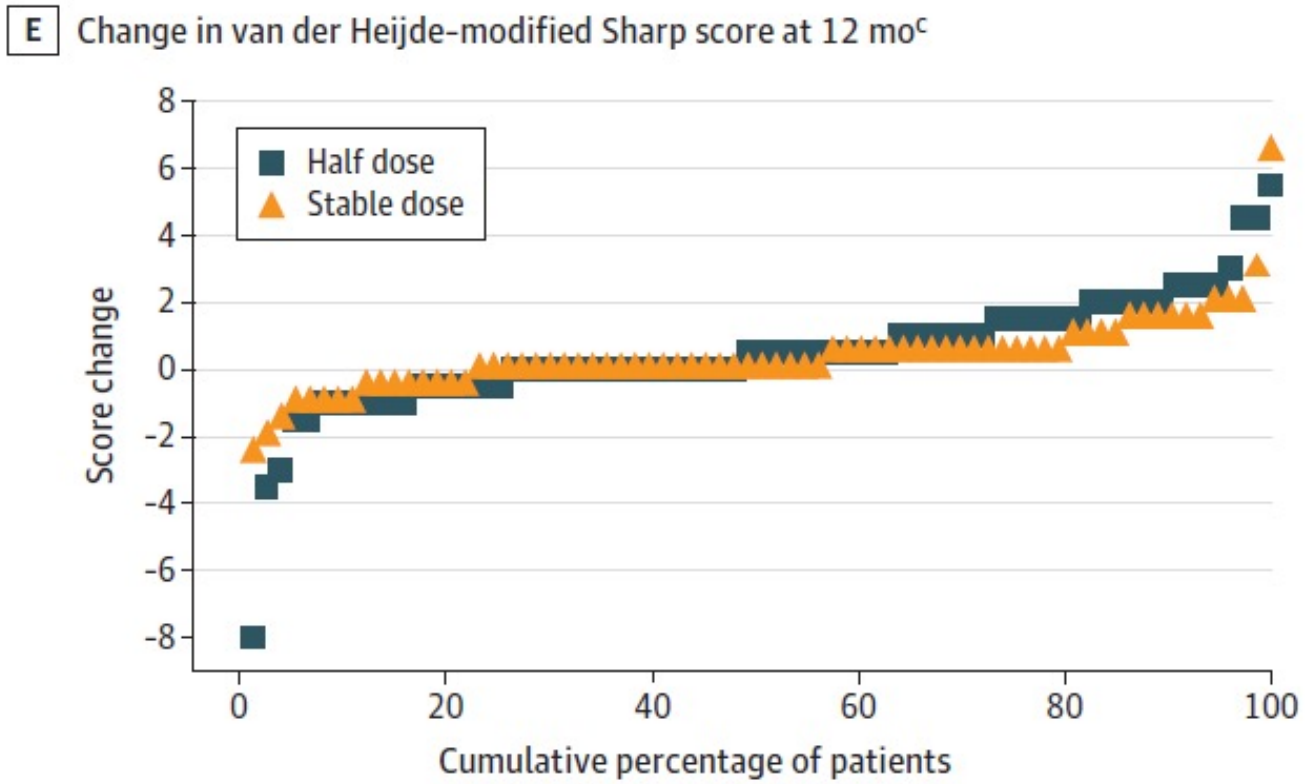
At least 1 flare at 1 year	
Stable dose	6.4%
Half dose	24.7%
ARI : 18.3% 95% CI : 0.069-0.295 P Value : 0.003	Statistically significant

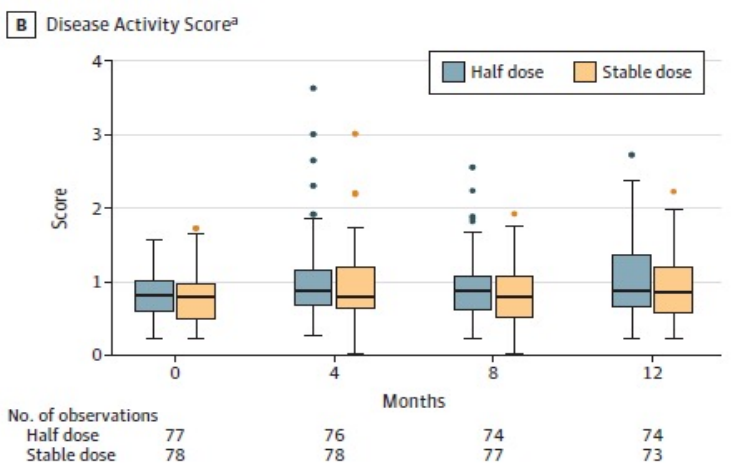
Result – Secondary

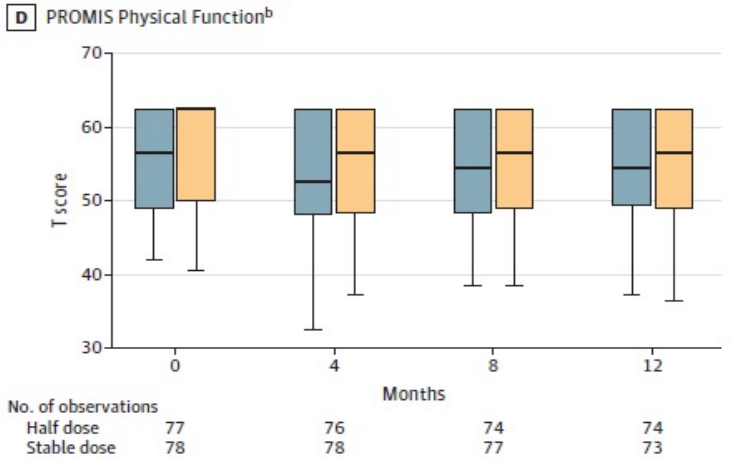


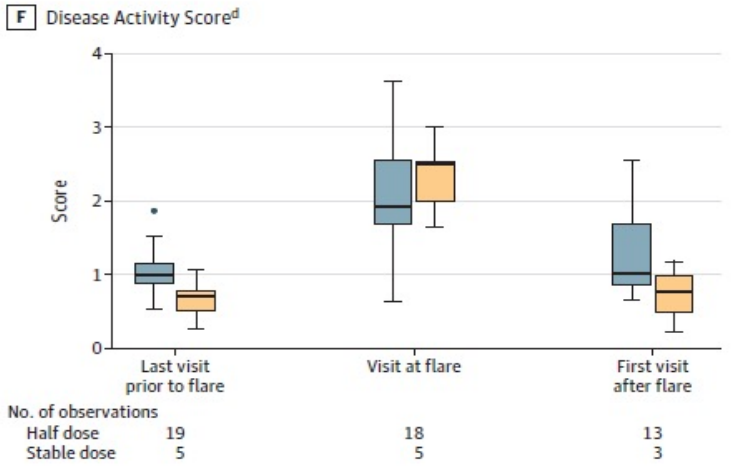
DAS remission at 1 year (DAS less than 1.6)	
Stable dose	92%
Half dose	85%
Difference: 7% 95% CI: -0.17-0.04	Statistically insignificant

Result – Secondary









Result – Adverse Events

	csDMARD group, No.	
	Half dose (n = 78)	Stable dose (n = 78)
Adverse events[a]		
Upper respiratory tract infections	11	13
Pneumonia	4	2
Back pain (including disk herniation)	3	1
Palpitations	3	2
Upper respiratory tract symptoms	3	4
Influenza	2	3
Joint pain	2	3
Dyspepsia	1	3
Nausea	1	3
Tooth infection/inflammation	0	3
Patients with adverse event, No. (%)		
1	20 (25)	17 (22)
≥2	14 (18)	25 (32)
Adverse events		
Serious[b,c]	4	2
Total	54	75

	Half dose	Stable dose
Any AE	69.2%	96.1%
Serious AE	5.1%	2.6%
Common AE		
Upper respiratory tract infection	14.1%	16.6%

Conclusion

Half dose csDMARD group		
Efficacy	X	Increase flare rate 18.3%, 1 year HR: 4
Adverse event	X	Despite lower any AE rate, but no difference in serious AE and common AE
Noninferiority	X	95 % CI cross the preset 20% noninferiority margin
Limitation	V	Open-label with some outcome assessment being subjective

- Half dose csDMARD therapy in patients with RA in remission is not supported

JAMA

Effect of Bamlanivimab vs Placebo on Incidence of COVID-19 Among Residents and Staff of Skilled Nursing and Assisted Living Facilities

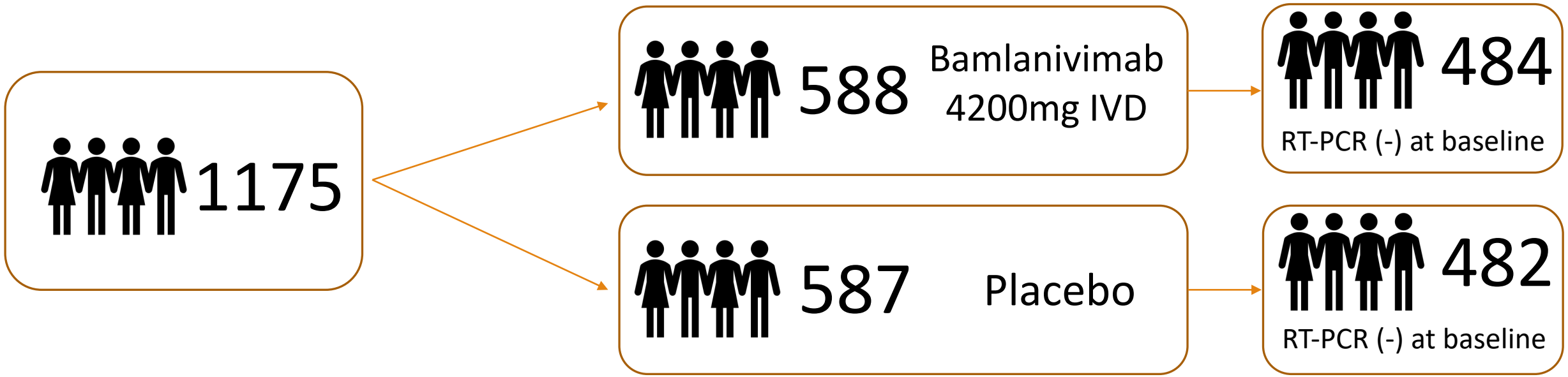
看使用Bamlanivimab的照護機構住民與照顧者對於預防COVID-19的感染與演變成非輕症的效果

Effect of Bamlanivimab vs Placebo on Incidence of COVID-19 Among Residents and Staff of Skilled Nursing and Assisted Living Facilities

Inclusion criteria
• > 18 years • Confirmed case of direct SARS-CoV-2 detection ≤7 days prior to randomization
Exclusion criteria
• Recovered from confirmed COVID-19 disease • History of a positive SARS-CoV-2 serology test • History of Convalescent COVID-19 plasma treatment • Previous SARS-CoV-2 vaccine trial • Previous receipt of SARS-CoV-2-specific monoclonal antibodies

- Randomized
- Double-Blind
- Phase III
- US
- Multi center
- 2020.8.2-2020.11.20
- Evaluation 8 weeks
- Follow-up 24 weeks
- mITT analysis

Randomization and Interventions



Characteristics of prevention group

Characteristics	Residents		Staff	
	Bamlanivimab (n = 161)	Placebo (n = 139)	Bamlanivimab (n = 323)	Placebo (n = 343)
Age				
Median (range), y	76.0 (31-104)	75.0 (41-96)	43.0 (18-82)	42.0 (18-74)
No. (%) ≥65 y	126 (78.3)	109 (78.4)	19 (5.9)	28 (8.2)
Sex, No. (%)				
Female	95 (59.0)	84 (60.4)	260 (80.5)	283 (82.5)
Male	66 (41.0)	55 (39.6)	63 (19.5)	60 (17.5)
Race, No./total (%)[b]				
White	145/160 (90.6)	126/138 (91.3)	284/322 (88.2)	303/340 (89.1)
Black or African American	13/160 (8.1)	11/138 (8.0)	25/322 (7.8)	30/340 (8.8)
American Indian or Alaska Native	0	0	4/322 (1.2)	1/340 (0.3)
Asian	1/160 (0.6)	0	5/322 (1.6)	5/340 (1.5)
Native Hawaiian or other Pacific Islander	1/160 (0.6)	0	1/322 (0.3)	1/340 (0.3)
Multiple	0	1/138 (0.7)	3/322 (0.9)	0
Hispanic or Latino ethnicity, No./total (%)[b]	3/160 (1.9)	7/139 (5.0)	17/323 (5.3)	21/343 (6.1)
Body mass index, median (range)[c]	28.2 (15.4-64.7)	29.1 (14.1-77.4)	29.9 (16.4-62.0)	30.3 (16.5-65.7)
At high risk of severe COVID-19, No. (%)[d]	161 (100)	139 (100)	132 (40.9)	143 (41.7)

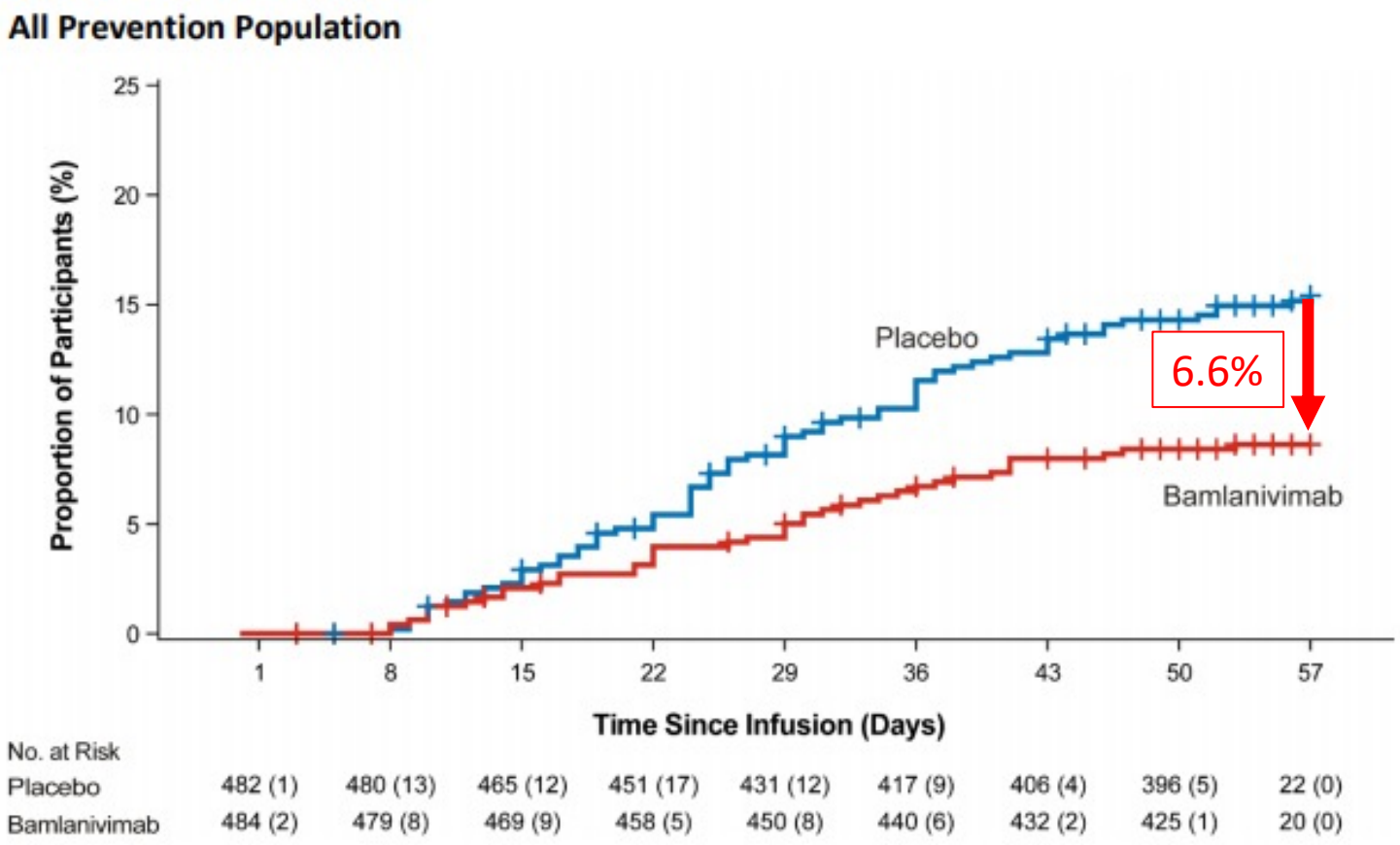
High Risk of severe COVID-19

Residents	100%
Staff	41.29%

Median age

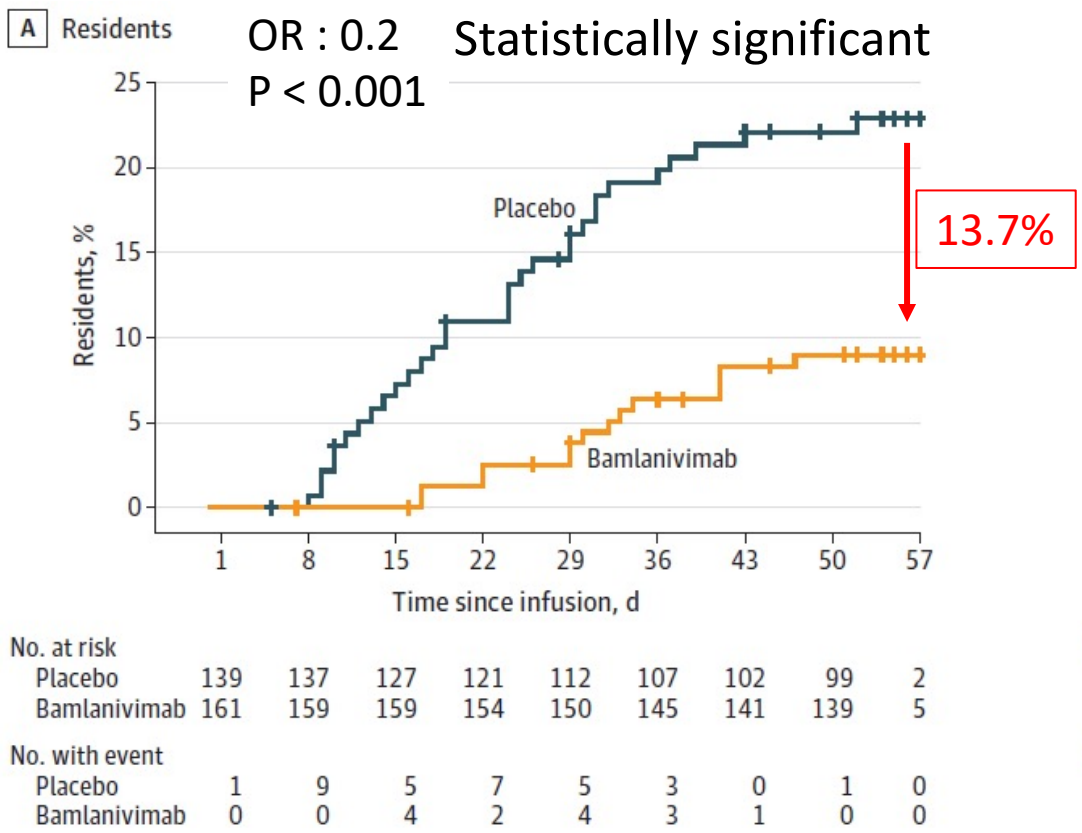
Residents	Bamlanivimab: 76 Placebo: 75
Staff	Bamlanivimab: 43 Placebo: 42

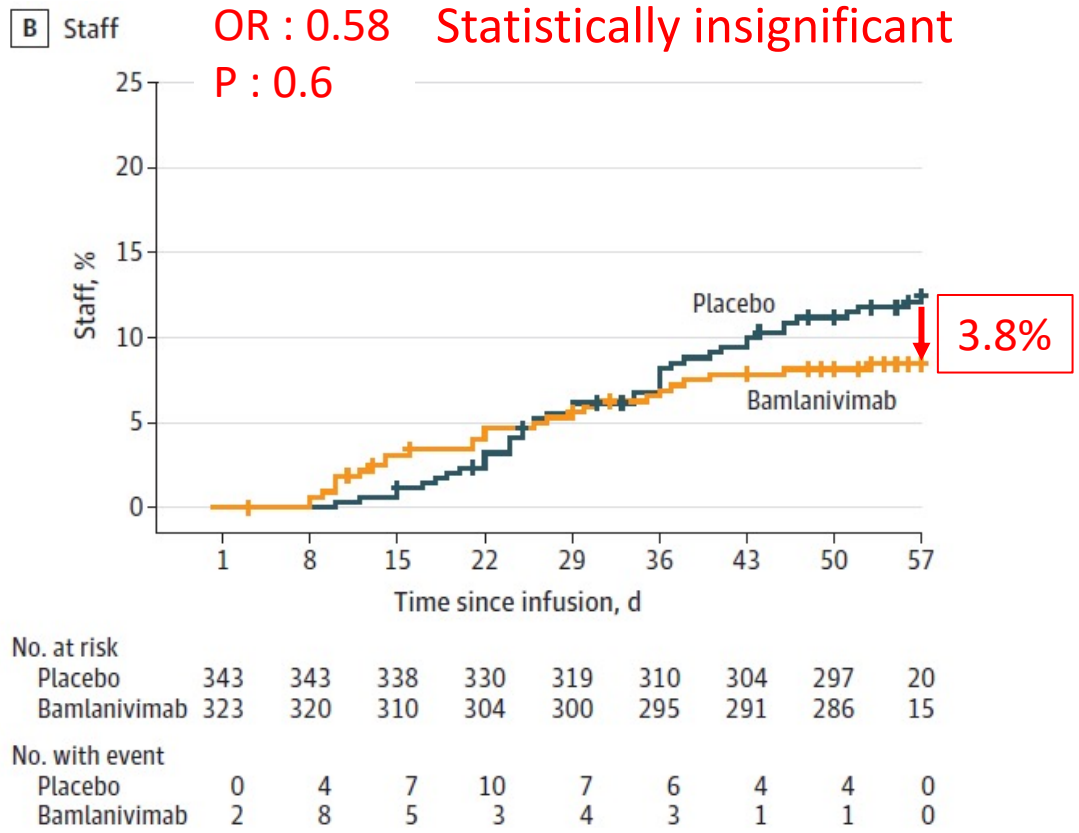
Result – Primary



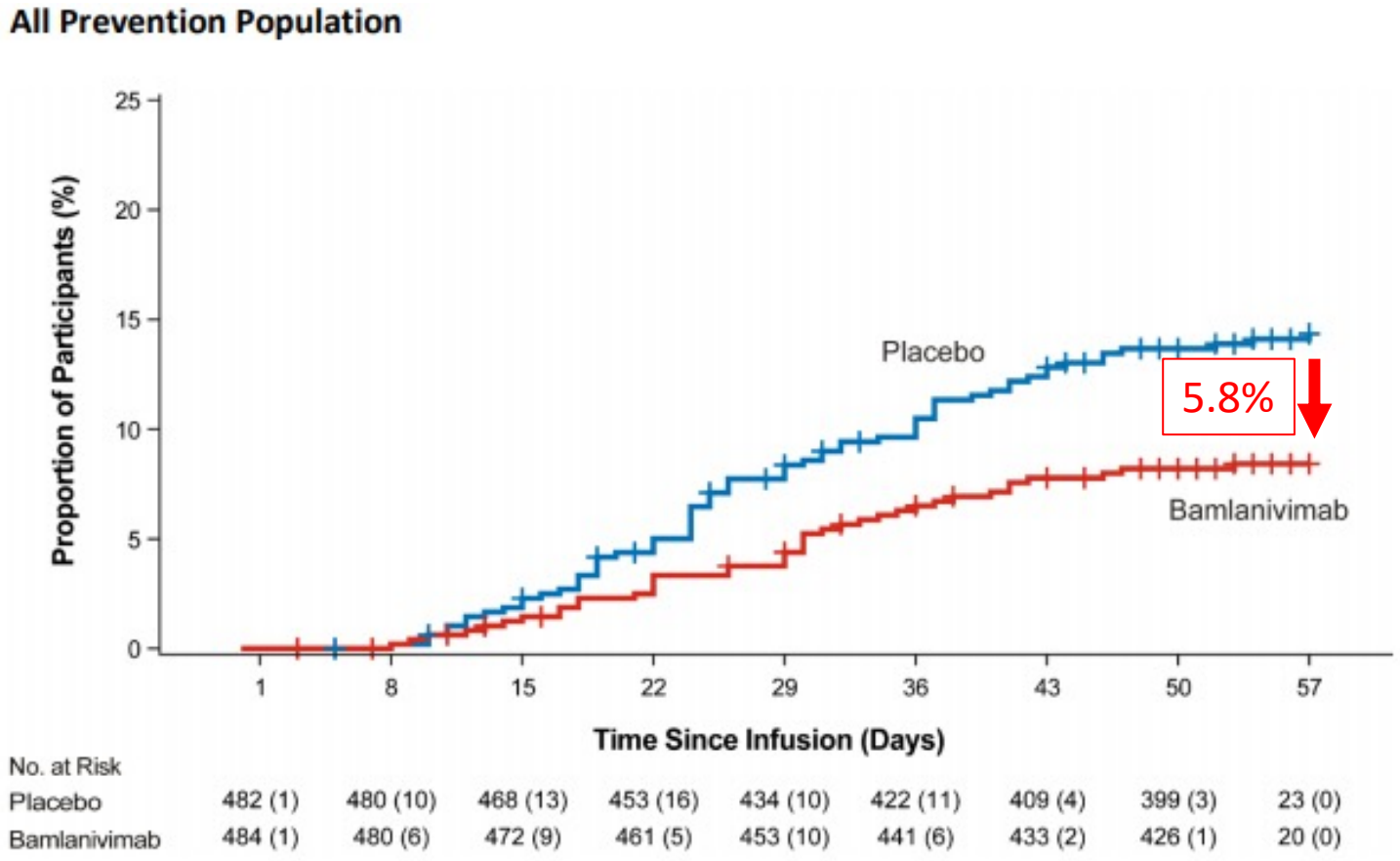
Mild or worse COVID-19 incident	
Bamlanivimab	8.5%
Placebo	15.2%
ARR: 6.6% OR : 0.43 95% CI : 0.28-0.68 P Value < 0.001	Statistically significant

Result – Primary





Result – Secondary



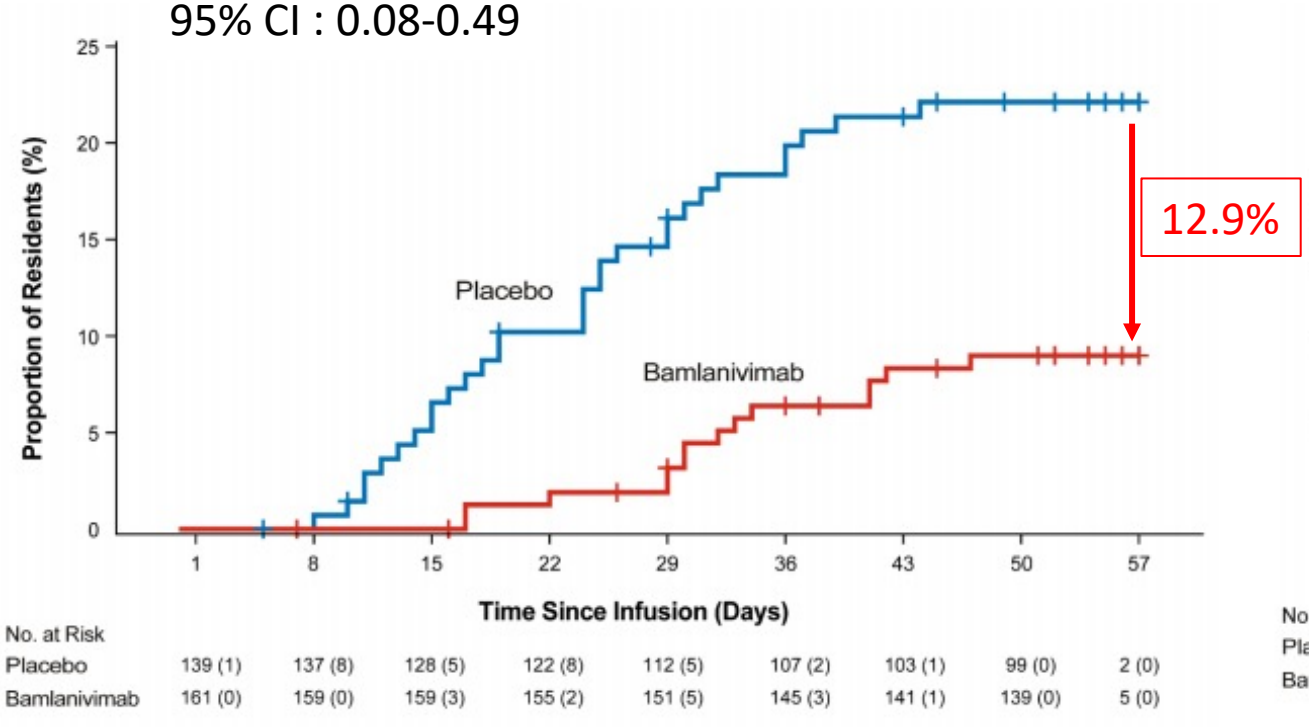
Moderate or worse COVID-19 incident	
Bamlanivimab	8.3%
Placebo	14.1%
ARR: 5.8% OR : 0.46 95% CI : 0.29-0.73 P Value < 0.001	Statistically significant

Result – Secondary

Residents

OR : 0.2
95% CI : 0.08-0.49

Statistically significant

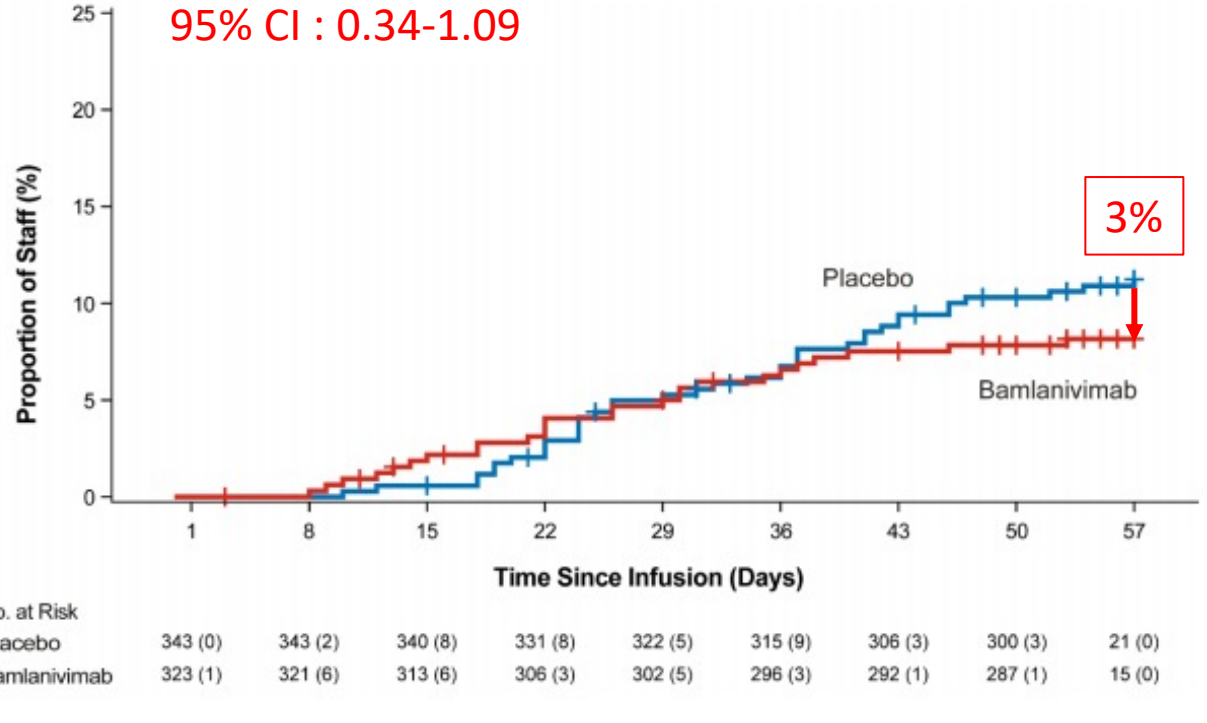


No. at Risk									
Placebo	139 (1)	137 (8)	128 (5)	122 (8)	112 (5)	107 (2)	103 (1)	99 (0)	2 (0)
Bamlanivimab	161 (0)	159 (0)	159 (3)	155 (2)	151 (5)	145 (3)	141 (1)	139 (0)	5 (0)

Staff

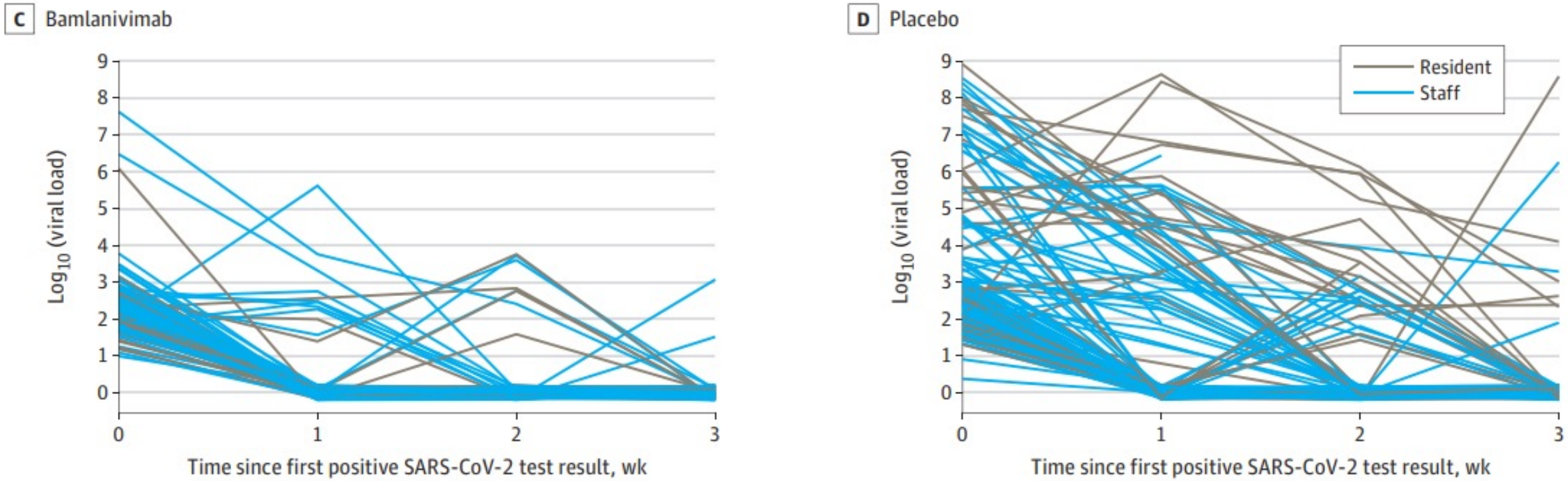
OR : 0.61
95% CI : 0.34-1.09

Statistically insignificant

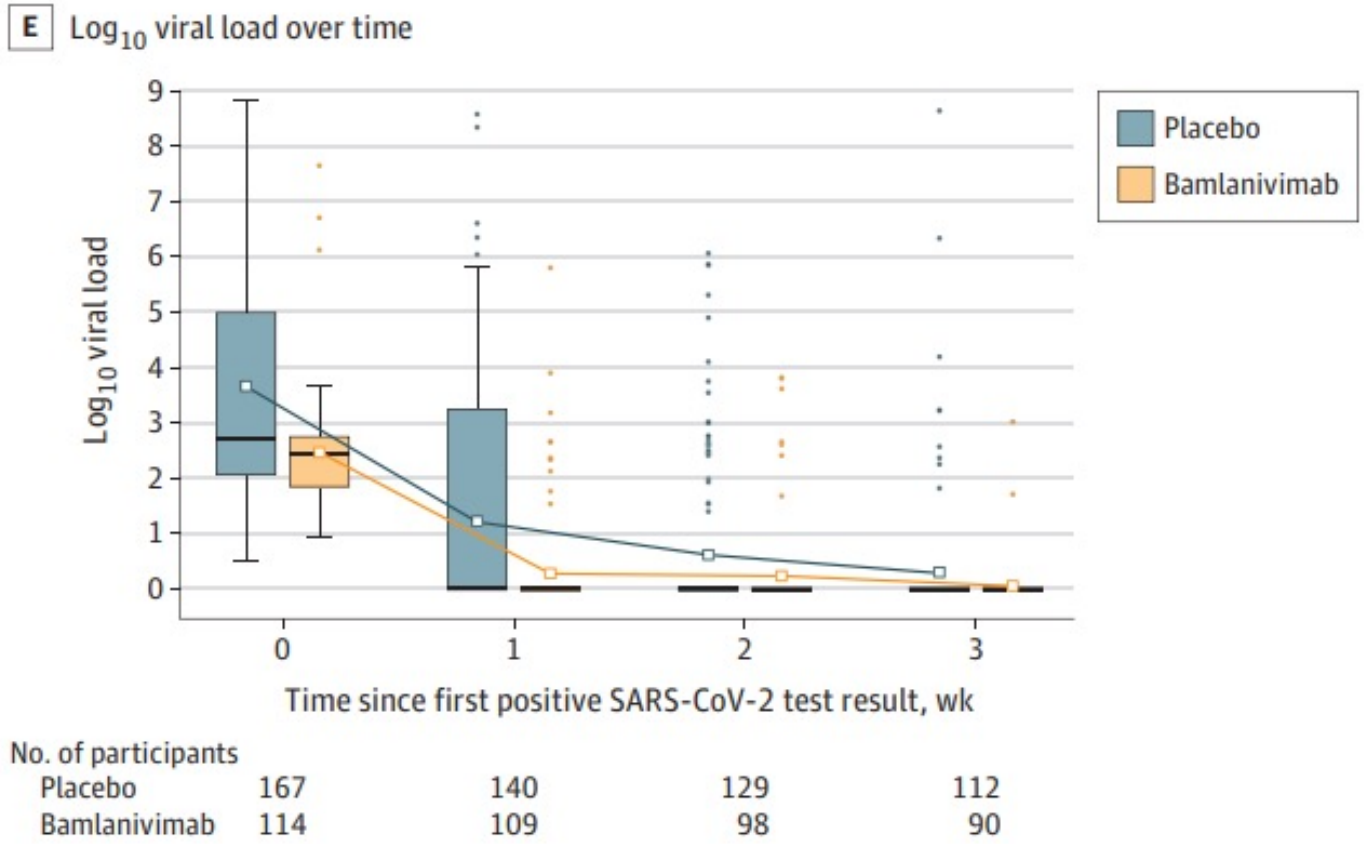


No. at Risk									
Placebo	343 (0)	343 (2)	340 (8)	331 (8)	322 (5)	315 (9)	306 (3)	300 (3)	21 (0)
Bamlanivimab	323 (1)	321 (6)	313 (6)	306 (3)	302 (5)	296 (3)	292 (1)	287 (1)	15 (0)

Result – Exploratory



Result – Exploratory



Result – Adverse Events

Adverse events[a]	No. (%) Bamlanivimab (n = 588)	Placebo (n = 587)
Participants with ≥1 treatment-emergent adverse event[b]	118 (20.1)	111 (18.9)
Severity of treatment-emergent adverse event[b,c]		
Severe	19 (3.2)	17 (2.9)
Moderate	29 (4.9)	31 (5.3)
Mild	66 (11.2)	61 (10.4)
Most common treatment-emergent adverse events (occurring in ≥1% of bamlanivimab or placebo recipients)[d]		
Urinary tract infection	12 (2.0)	14 (2.4)
Hypertension	7 (1.2)	10 (1.7)
Fall	2 (0.3)	6 (1.0)
Dizziness	4 (0.7)	6 (1.0)
Arthralgia	6 (1.0)	4 (0.7)
Serious adverse events[e]	22 (3.7)	19 (3.2)
Deaths resulting from adverse event[f]	5 (0.9)	6 (1.0)
Discontinuation from study participation due to adverse event (including death)	5 (0.9)	6 (1.0)

	Bamlanivimab	Placebo
TEAE	20.1%	18.9%
Serious AE	3.7%	3.2%
Death form AE	0.9%	1%

Conclusion

Bamlanivimab group		
Efficacy	V	Reduce mild incident 6.6% and moderate incident 5.8% Better efficacy at resident (high age, high risk) group
Adverse event	V	Despite higher at TEAE rate, but no difference in serious AE and common AE
Limitation	V	A variety of SARS-CoV-2 variants have recently been identified outside of this study Little racial diversity in the participant population

- Treatment with Bamlanivimab monotherapy can reduce the incidence of COVID-19 infection
- Reduce incident of mild to moderate symptoms if infected
- Whether Bamlanivimab affect COVID-19 vaccines performance are still unknown

US FDA revokes EUA of Bamlanivimab at 2021.04.16 due to E484K or L452R spike protein variant substitutions have large reductions in susceptibility to Bamlanivimab

JAMA

Association Between Administration of IL-6 Antagonists and Mortality Among Patients Hospitalized for COVID-19

看使用IL-6 antagonist對於感染COVID-19的住院病人死亡率的影響

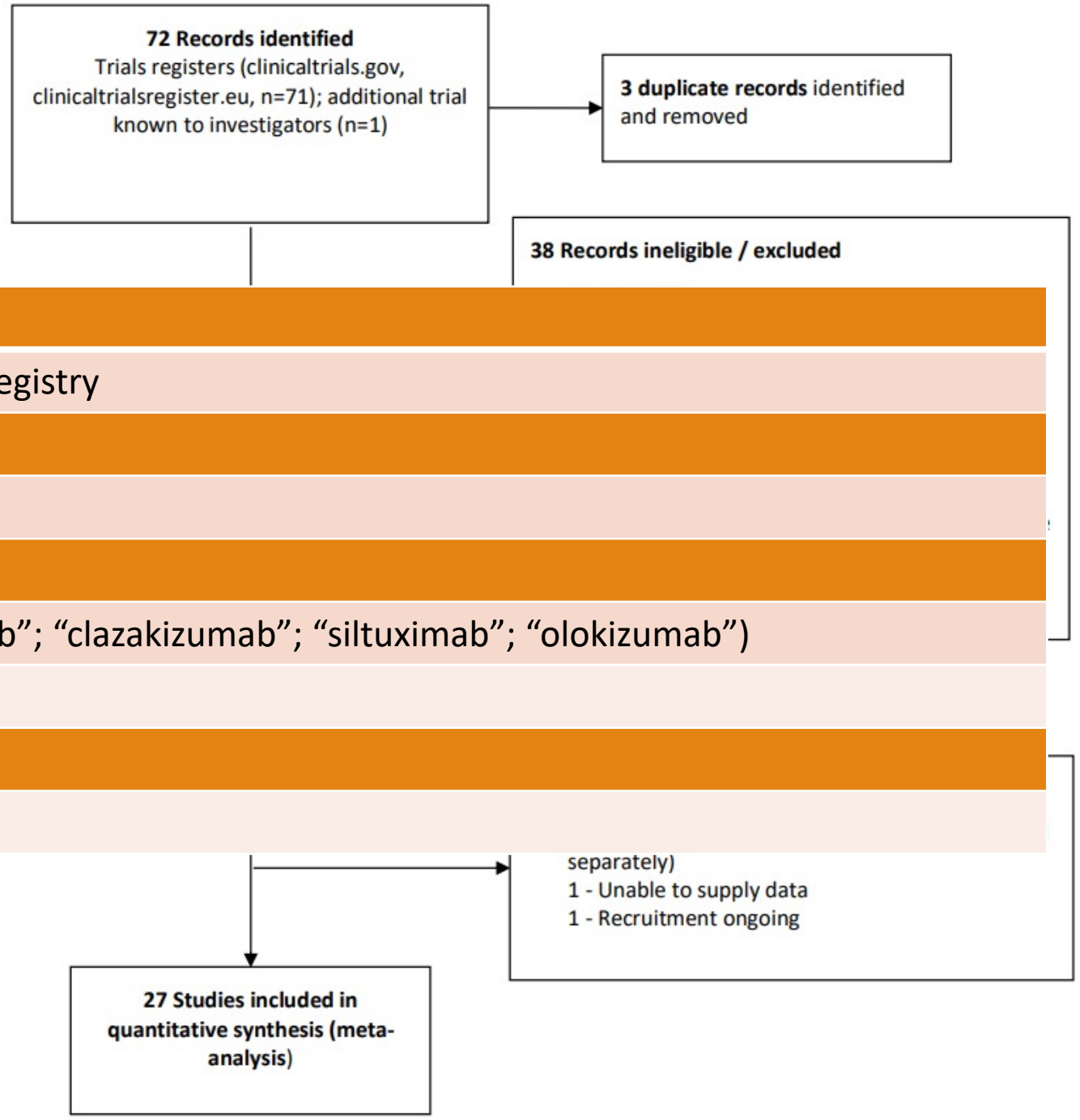
Association Between Administration of IL-6 Antagonists and Mortality Among Patients Hospitalized for COVID-19

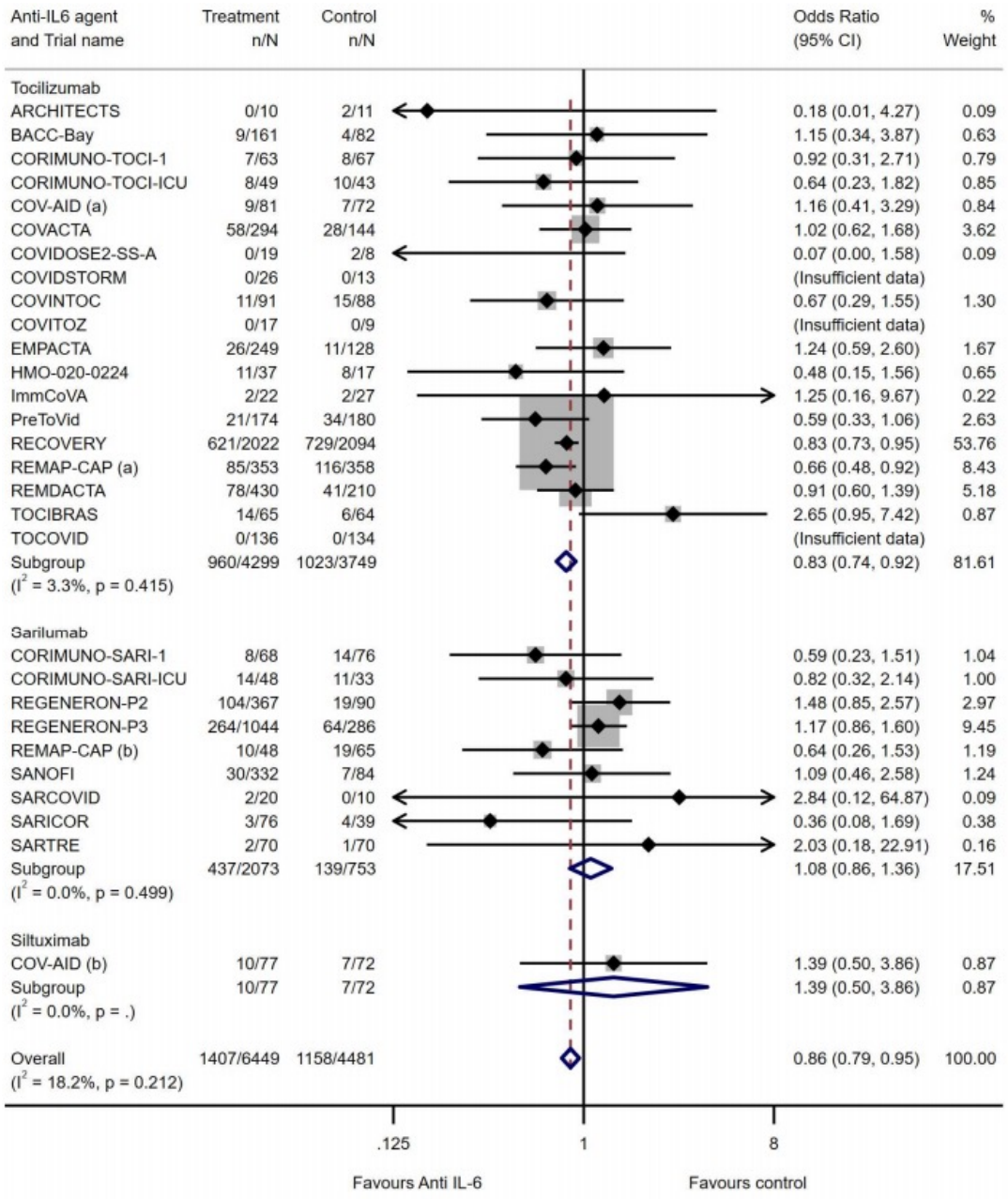
Eligibility criteria	
P	Hospitalized with suspected or proven COVID-19
I	Anti-IL-6 therapies
C	Usual care or placebo or systemic corticosteroids
O	All-cause mortality up to 28 days after randomization
Exclusion criteria	
P	Non-COVID trials or restricted to patients with advanced cancer
I	Anti- IL-6 therapies combined with other active agents
C	Active comparators other than systemic corticosteroids
O	

- Meta-analysis
- Only RCT included
- 27 studies
- No restriction on publication status and language

Search strategy

Database
clinicaltrials.gov, EudraCT, WHO ISRCTN registry
Title or Abstract term
“random” AND “COVID”
Terms
IL6-antagonists (“tocilizumab”; “sarilumab”; “clazakizumab”; “siltuximab”; “olokizumab”)
"Interleukin 6”
Search date
2020.10.17, 2020.11.25, 2021.01.11

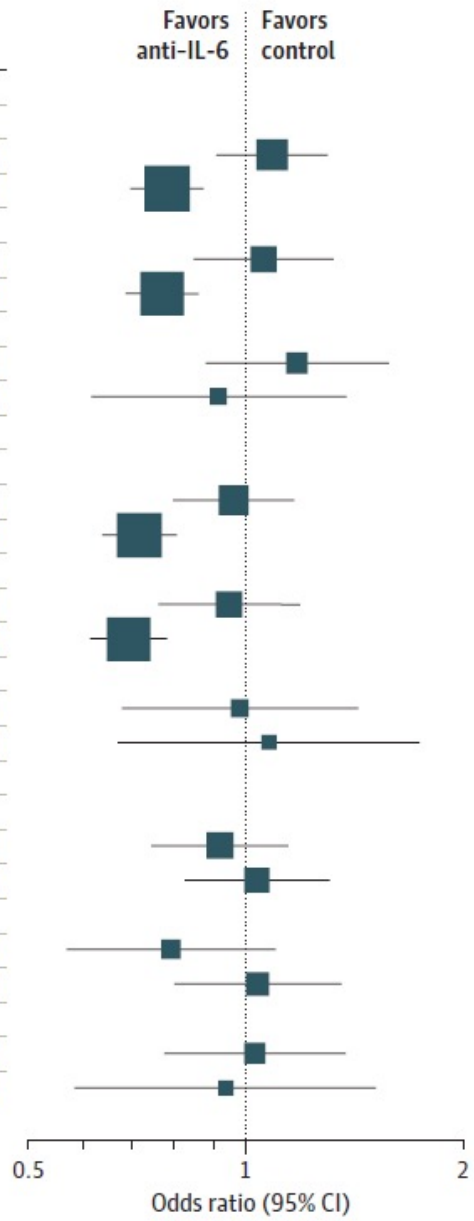




28 days all-cause mortality
Anti IL-6 VS Usual care or Placebo

Overall n=10930 I^2=18.2%	OR: 0.86 95% CI: 0.79 - 0.95
Tocilizumab n=8048 weight: 81.61% I^2=3.3%	OR: 0.83 95% CI: 0.74 - 0.92
Sarilumab n=2826 weight: 17.51% I^2=0	OR: 1.08 95% CI: 0.86 - 1.36
Siltuximab n=149 weight: 0.87% I^2=0	OR: 1.39 95% CI: 0.50 - 3.86

Outcome and treatment	I^2, %	No. of events/total patients		Odds ratio (95% CI)
		Control	Anti-IL-6	
28-d mortality				
All anti-IL-6				
No corticosteroid use	0	293/1280	537/2357	1.09 (0.91-1.30)
Corticosteroid use	0	838/2848	827/3468	0.78 (0.69-0.88)
Tocilizumab				
No corticosteroid use	0	211/898	254/1192	1.06 (0.85-1.33)
Corticosteroid use	0	793/2585	693/2815	0.77 (0.68-0.87)
Sarilumab				
No corticosteroid use	0	83/384	283/1134	1.18 (0.88-1.58)
Corticosteroid use	0	48/281	124/607	0.92 (0.61-1.38)
Progression to IMV, ECMO, or death at 28 d				
All anti-IL-6				
No corticosteroid use	0	308/1004	399/1541	0.96 (0.79-1.17)
Corticosteroid use	0	893/2496	822/2986	0.71 (0.63-0.80)
Tocilizumab				
No corticosteroid use	0	250/791	266/1016	0.95 (0.76-1.20)
Corticosteroid use	0	859/2283	729/2518	0.69 (0.61-0. 78)
Sarilumab				
No corticosteroid use	0	59/214	126/498	0.98 (0.67-1.44)
Corticosteroid use	0	38/227	75/423	1.08 (0.67-1.75)
28-d secondary infections[a]				
All anti-IL-6				
No corticosteroid use	3	165/758	434/1820	0.92 (0.74-1.15)
Corticosteroid use	1	160/798	310/1378	1.04 (0.82-1.31)
Tocilizumab				
No corticosteroid use	0	86/385	146/659	0.79 (0.57-1.10)
Corticosteroid use	16	132/573	210/772	1.04 (0.80-1.36)
Sarilumab				
No corticosteroid use	8	79/373	285/1130	1.03 (0. 77-1.38)
Corticosteroid use	0	28/225	92/560	0.94 (0.58-1.52)

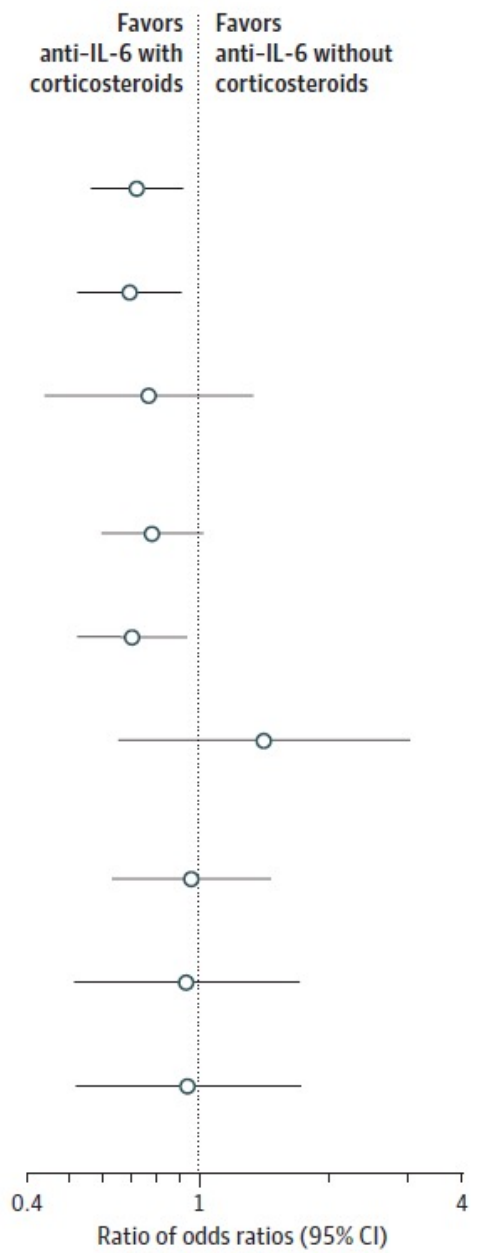


Subgroup analysis Corticosteroids

Anti IL-6 VS Usual care or Placebo

28-day mortality All anti IL-6	Steroid	No steroid
	OR: 0.78	OR: 1.09
Progression to IMV, ECMO, death All anti IL-6	Steroid	No steroid
	OR: 0.71	OR: 0.96
28-day secondary infection All anti IL-6	Steroid	No steroid
	OR: 1.04	OR: 0.79

Outcome and treatment	I^2, %	No. of events/total patients		Odds ratio (95% CI)	Ratio of odds ratios (95% CI)	I^2, %	P value
		Control	Anti-IL-6				
28-d mortality							
All anti-IL-6							
No corticosteroid use	0	293/1280	537/2357	1.09 (0.91-1.30)	0.72 (0.56-0.92)	0	.008
Corticosteroid use	0	838/2848	827/3468	0.78 (0.69-0.88)			
Tocilizumab							
No corticosteroid use	0	211/898	254/1192	1.06 (0.85-1.33)	0.69 (0.52-0.91)	0	.008
Corticosteroid use	0	793/2585	693/2815	0.77 (0.68-0.87)			
Sarilumab							
No corticosteroid use	0	83/384	283/1134	1.18 (0.88-1.58)	0.77 (0.44-1.33)	0	.34
Corticosteroid use	0	48/281	124/607	0.92 (0.61-1.38)			
Progression to IMV, ECMO, or death at 28 d							
All anti-IL-6							
No corticosteroid use	0	308/1004	399/1541	0.96 (0.79-1.17)	0.78 (0.59-1.02)	0	.07
Corticosteroid use	0	893/2496	822/2986	0.71 (0.63-0.80)			
Tocilizumab							
No corticosteroid use	0	250/791	266/1016	0.95 (0.76-1.20)	0.70 (0.52-0.94)	0	.02
Corticosteroid use	0	859/2283	729/2518	0.69 (0.61-0. 78)			
Sarilumab							
No corticosteroid use	0	59/214	126/498	0.98 (0.67-1.44)	1.41 (0.65-3.07)	0	.38
Corticosteroid use	0	38/227	75/423	1.08 (0.67-1.75)			
28-d secondary infections[a]							
All anti-IL-6							
No corticosteroid use	3	165/758	434/1820	0.92 (0.74-1.15)	0.96 (0.63-1.46)	0	.85
Corticosteroid use	1	160/798	310/1378	1.04 (0.82-1.31)			
Tocilizumab							
No corticosteroid use	0	86/385	146/659	0.79 (0.57-1.10)	0.94 (0.51-1.71)	11	.83
Corticosteroid use	16	132/573	210/772	1.04 (0.80-1.36)			
Sarilumab							
No corticosteroid use	8	79/373	285/1130	1.03 (0. 77-1.38)	0.94 (0.52-1.72)	6	.85
Corticosteroid use	0	28/225	92/560	0.94 (0.58-1.52)			



Critical Inhaler Administration Errors of Patients on Pressurized Meter Dose Inhaler (pMDI): A Hospital-Based Cross-Sectional Study in Malaysia

hospital pharmacy

分析使用pMDI容易發生錯誤的步驟與族群

Critical Inhaler Administration Errors of Patients on Pressurized Meter Dose Inhaler (pMDI): A Hospital-Based Cross-Sectional Study in Malaysia

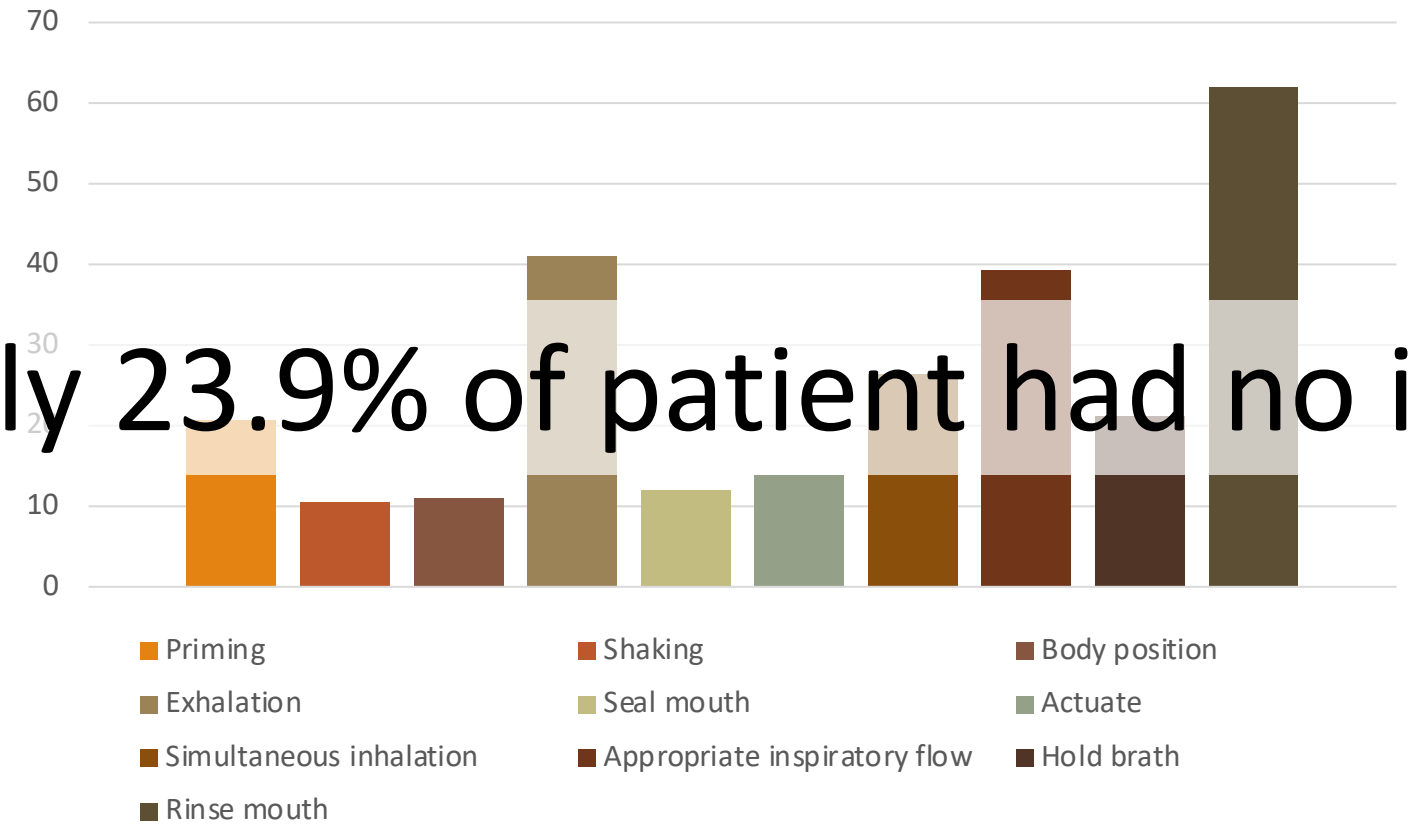
Inclusion criteria
• Asthma • COPD • Over 18 years • Use of at least 1 pMDI with out spacer or facemask
Exclusion criteria
• Additional respiratory disease • Influenza-like-illness

- Cross-Sectional
- Observational
- Multi center
- 209 patient included

Demographics

- Asthma: 55.5%
- Mean age: 58.5
- Male: 56.5%
- Smoker/ex-smoker: 49.1%
- Using pMDI for more than 10 years: 33.7%
- Have 2 inhaler devices: 68.9%
- Attended a prior asthma education: 34.0%

Result



Top 3 error

1. 用ICS忘了漱口
2. 用之前氣沒吐乾淨
3. 吸氣流量不對

Only 23.9% of patient had no inhalation error

Result

Table 3. Characteristics of Patients Making At Least One Critical Error and Patients Making No Errors.

	All patients N (%)	Patients making at least one critical error n = 124	Patients making no critical error n = 85	*P*-value
Patient age,[a] mean ± SD	58.51 ± 15.46	55.01 ± 15.45	60.90 ± 15.06	.007*
Gender[b]				.556
Male	118 (56.46)	70	48	
Education[b]				.001*
No formal education	17 (8.1)	14	3	
Primary	57 (27.3)	38	19	
History of inhaler use[b]				.242
Less than a year	31 (15.3)	15	16	
1-5 years	72 (35.6)	47	25	
6-10 years	31 (15.3)	21	10	
More than 10 years	68 (33.7)	37	31	
Missing data	7 (3.3)	–	–	
Semi-dependent	126 (60.3)	82	44	
Dependent	16 (7.6)	5	11	
Missing data	12 (5.7)	–	–	
Prior counseling[b]				.521
Yes	73 (34.0)	30	43	
No	136 (60.3)	55	81	

Conclusion

Majority of patients on pMDI make inhalation errors

lower education level, advanced age, lack of understanding of their medication use are at a greater risk of committing critical errors

Clinical Validity Assessment of Integrated Dose Range Checking Tool in a Tertiary Care Hospital Using an Electronic Health Information System

hospital pharmacy

分析CDSS中的劑量評估工具所發出警告的成效

Clinical Validity Assessment of Integrated Dose Range Checking Tool in a Tertiary Care Hospital Using an Electronic Health Information System

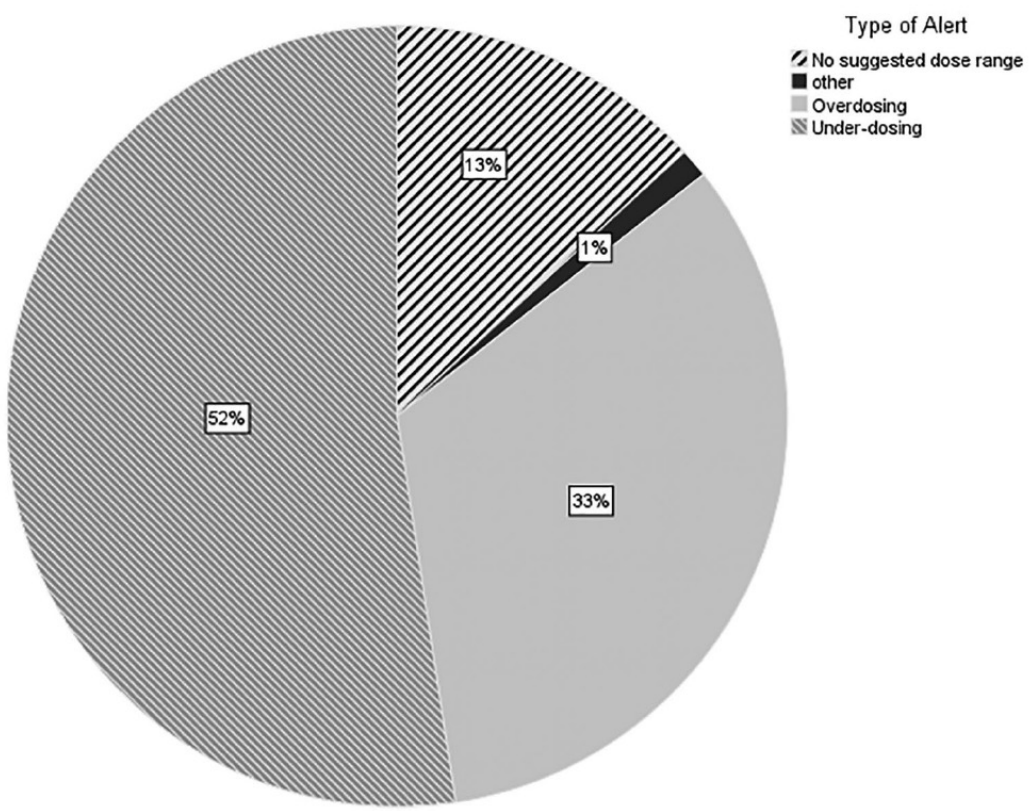
Data source
• Inpatient DRC alert • First 300 alert of the day • Institutional formulary
End points
• Clinically valid alert • Overridden alert • Accepted alert • Implemented alerts

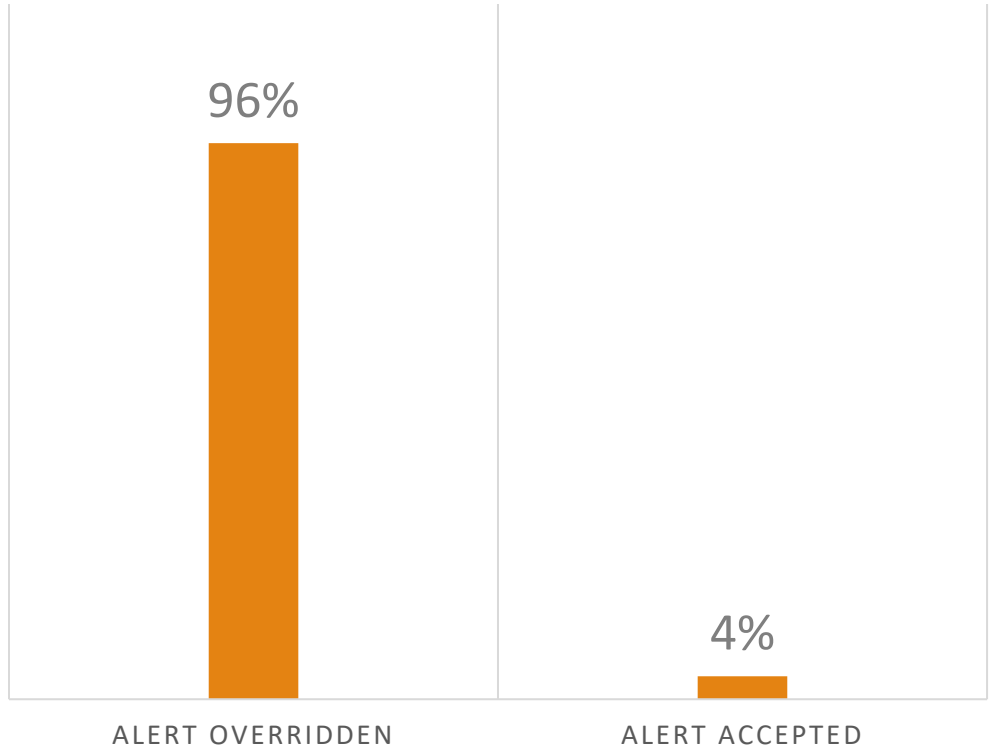
- Retrospective
- Observational
- 10 days
- 3000 alerts were gathered

Result

Characteristic	N = 3000
Age category	
Adult	1659 (55%)
Pediatric	1341 (45%)
Gender	
Male	1586 (53%)
Female	1414 (47%)
Renal function	
Alerted medications that needed renal adjustments	1557 (52%)
Patients who have any level of renal failure	398 (13%)
Liver function	
Alerted medications that needed liver adjustments	708 (24%)
Patients who have any level of liver failure	89 (3%)
Nursing unit category	
Medical units	2359 (79%)
Critical unit	641 (21%)
Position of the health care provider who received the alerts	
Pharmacist	1171 (39%)
Medical resident	706 (24%)
Assistant physician	693 (23%)
Fellow	375 (12%)
Consultant	55 (2%)

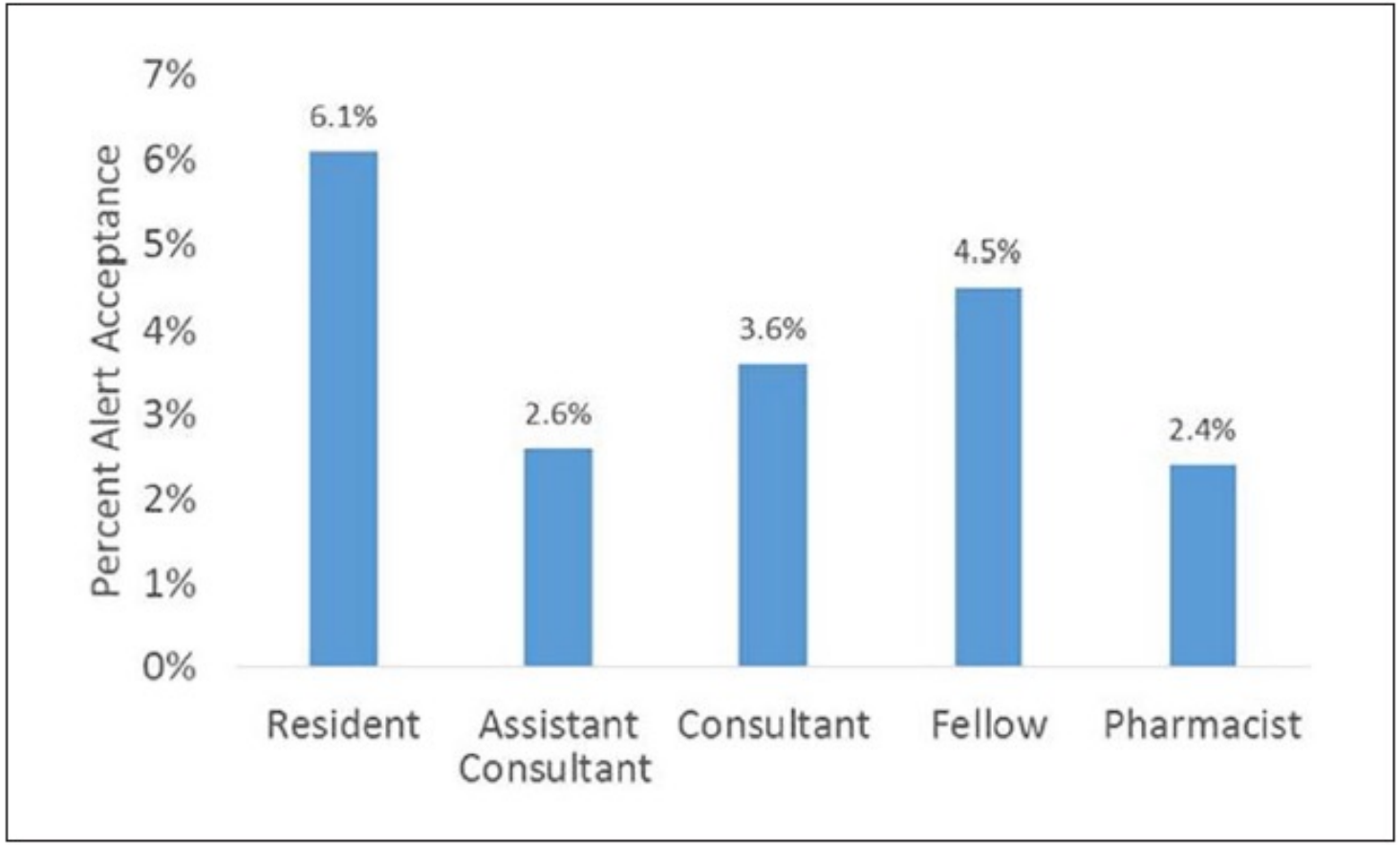
Result



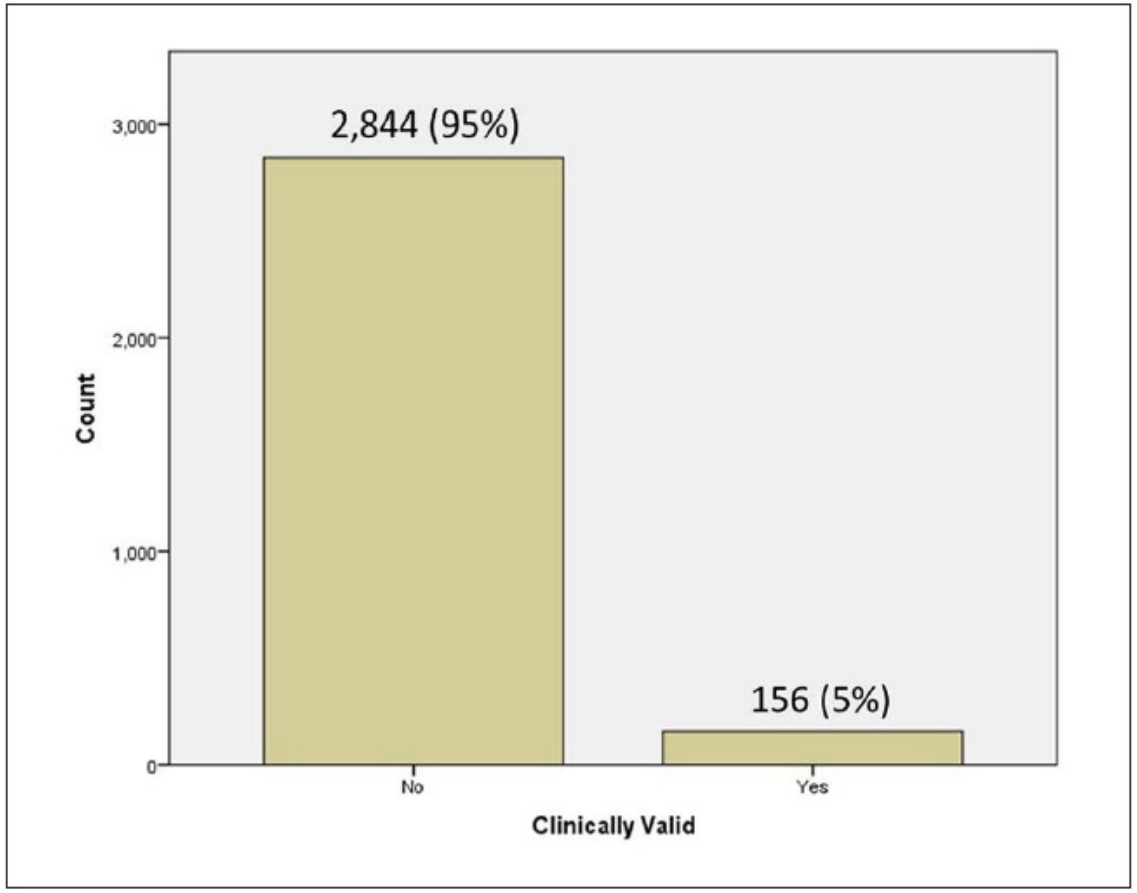


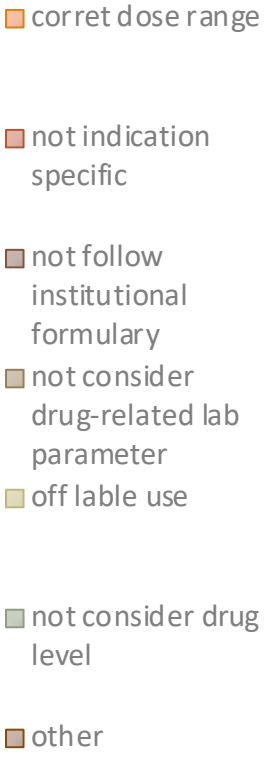
Only 10% of the accepted alert were implemented

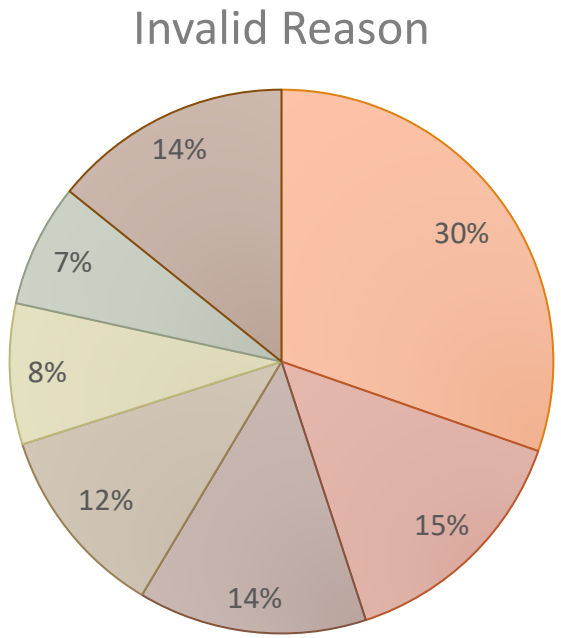
Result


Percent Alert Acceptance
7%
6%
5%
4%
3%
2%
1%
0%
6.1%
2.6%
3.6%
4.5%
2.4%
Resident
Assistant Consultant
Consultant
Fellow
Pharmacist

Result


2,844 (95%)
156 (5%)
3,000
2,000
1,000
0
Count
No
Yes
Clinically Valid


corret dose range
not indication specific
not follow institutional formulary
not consider drug-related lab parameter
off lable use
not consider drug level
other


Invalid Reason
14%
30%
7%
8%
12%
15%
14%

Conclusion

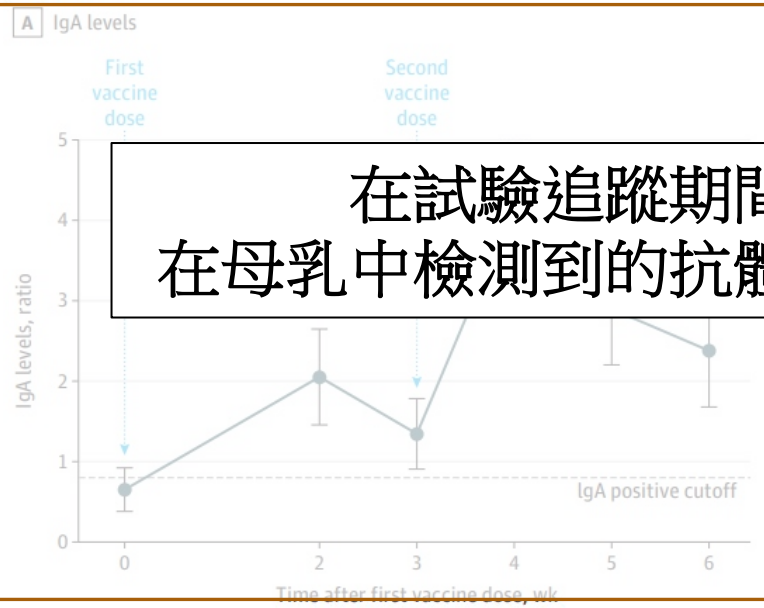
- Traditional DRC function as an integrated clinical decision support tool yielded invalid clinical recommendations in most of the cases. This can contribute to inappropriate recommendation adaptation.
- Alert fatigue may occur.
- DRC function should consider customization for patient specific dosing factors.

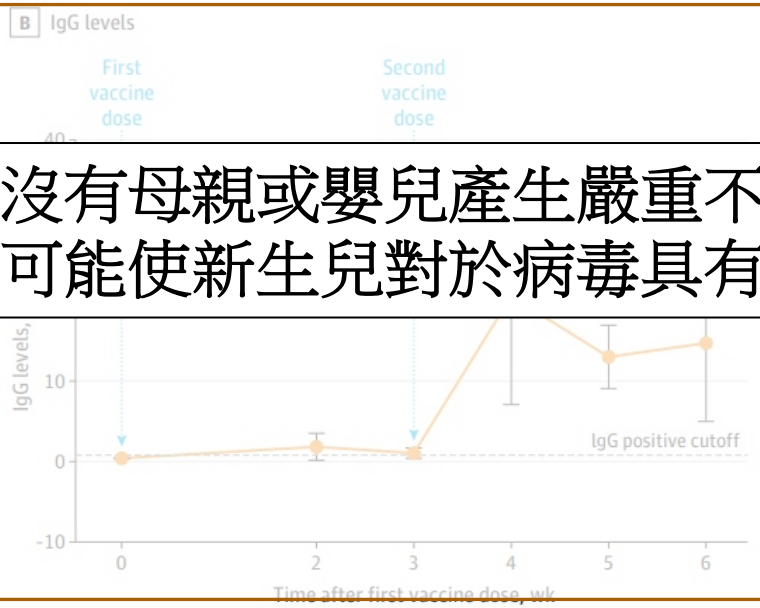
Abstract

SARS-CoV-2–Specific Antibodies in Breast Milk After COVID-19 Vaccination of Breastfeeding Women

P	Breastfeeding women
I	2 doses of the Pfizer-BioNTech vaccine 21 days apart
C	None
O	Levels of IgA and IgG in Breast Milk

- Prospective cohort
- Israel
- 2020.12.23-2021.1.15





在試驗追蹤期間沒有母親或嬰兒產生嚴重不良反應
在母乳中檢測到的抗體可能使新生兒對於病毒具有一定的防護力

Adverse events

	her	infant
		0
fever	10	4
most common	Local pain	

Association of Intravenous Immunoglobulins Plus Methylprednisolone vs Immunoglobulins Alone With Course of Fever in Multisystem Inflammatory Syndrome in Children

P	0-19 years with confirmed MIS-C associated with SARSCoV-2 infection
I	IVIG 2g/Kg + methylprednisolone 0.8-1mg/Kg Q12H
C	IVIG 2g/Kg
O	Persistence of fever for 2 days, recrudescence of fever within 7 days after the initial therapy

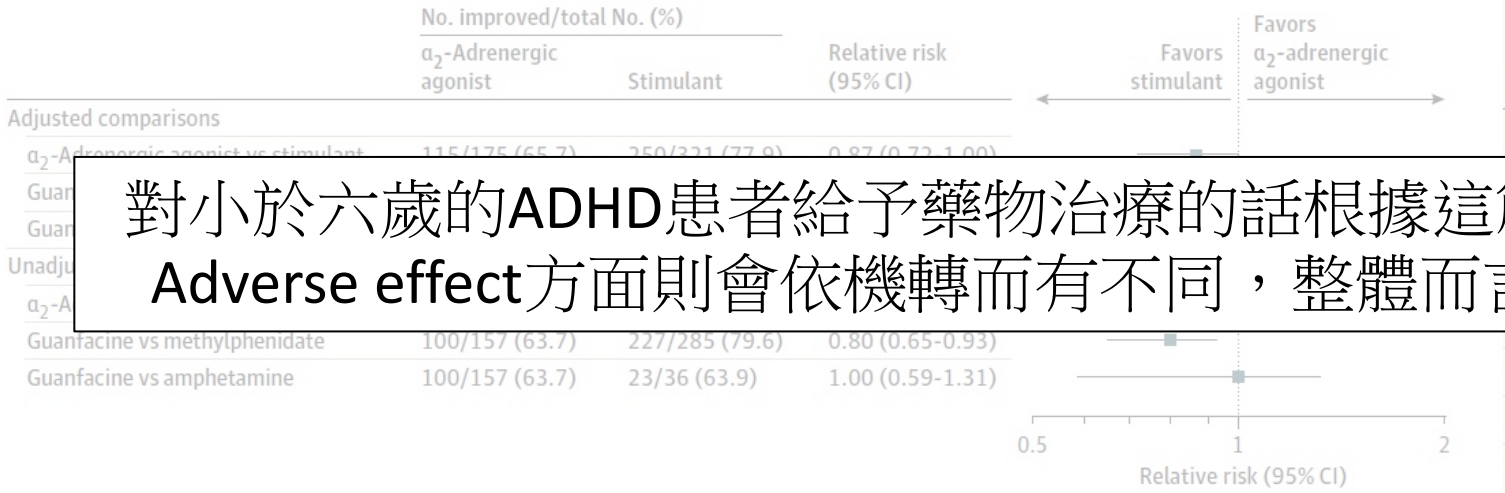
- Retrospective cohort
- Observational
- French
- 2020.4.1-2021.1.6

IVIG併用類固醇可以降低發生treatment failure的機會，縮短發燒的時間
但由於是observational study 所以interpretation會受限

α2-Adrenergic Agonists or Stimulants for Preschool-Age Children With Attention-Deficit/Hyperactivity Disorder

P	Less than 6 years, ADHD diagnosis by a developmental-behavioral pediatrician
I	α2-adrenergic agonist (clonidine, guanfacine)
C	Stimulant (methylphenidate, amphetamine)
O	Improvement of ADHD symptom (CGI-I score), adverse events

- Retrospective
- Record review
- 2013.1.1-2017.7.1
- At least 20-month follow-up



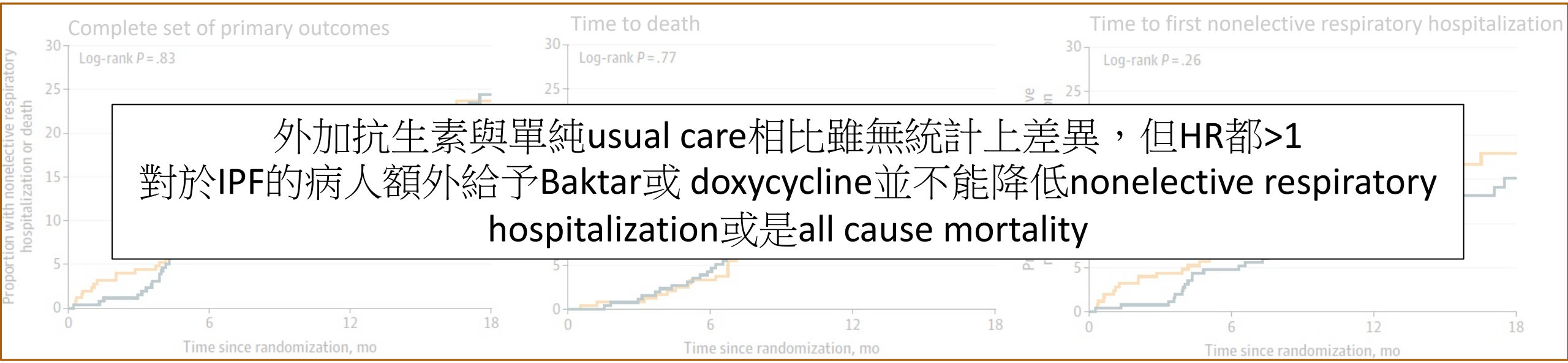
對小於六歲的ADHD患者給予藥物治療的話根據這篇研究是favor stimulants的Adverse effect方面則會依機轉而有不同，整體而言stimulants的AE較常發生

Adverse effect[a]	No. (%) [95% CI] α2-Adrenergic agonist (n = 175)	Stimulants (n = 321)[b]
Daytime sleepiness	66 (38) [30-45]	9 (3) [1-5]
Appetite suppression	13 (7) [3-12]	123 (38) [33-44]
Stomachaches	8 (5) [1-8]	42 (13) [9-17]
Skin picking or other repetitive behaviors	8 (5) [1-8]	36 (11) [7-15]

Effect of Antimicrobial Therapy on Respiratory Hospitalization or Death in Adults With Idiopathic Pulmonary Fibrosis

P	≥ 40 years with IPF diagnosis
I	Antibiotic (Baktar or doxycycline) plus usual care
C	Usual care
O	First nonelective respiratory hospitalization or all cause mortality

- Randomized
- Opel-label
- Median follow-up 12.7 month



外加抗生素與單純usual care相比雖無統計上差異，但HR都>1
對於IPF的病人額外給予Baktar或 doxycycline並不能降低nonelective respiratory hospitalization或是all cause mortality

A Real-World Comparative Effectiveness Analysis of Thromboprophylactic Use of Enoxaparin Versus Unfractionated Heparin in Abdominal Surgery Patients in a Large U.S. Hospital Database

P	Hospitalized patients (>18 years) undergoing selected abdominal surgeries
I	At least 1 day with ≤40 mg of enoxaparin
C	At least 1 day with ≤15 000 IU of UFH
O	VTE, all-cause in hospital death, PE hospital death

- Retrospective
- Observational
- US
- 2010.1.1 – 2016.9.30

使用**enoxaparin**可能可以降低在住院期間發生**VTE**的機會以及降低住院期間的死亡率
但出院後的**followup**兩者並無顯著差異

	Unadjusted analyses			Adjusted analyses
				Odds Ratio[a] for Enoxaparin
Mortality	821 (0.38)	936 (0.63)	<.001	0.67 (0.60-0.75)
PE-related mortality	17 (0.01)	18 (0.01)	.22	0.67 (0.33-1.35)
Outcomes during 90 d following index discharge	N = 74 053	N = 50 655		
VTE	1323 (1.79)	967 (1.91)	.11	0.93 (0.85-1.01)
Mortality	713 (0.96)	529 (1.04)	.15	0.96 (0.84-1.08)
PE-related mortality	41 (0.06)	36 (0.07)	.27	0.76 (0.47-1.24)

Standard- versus High-Dose Dexmedetomidine for Sedation in the Intensive Care Unit

P	Patient required mechanical ventilation for at least 24 hours dexmedetomidine as initial monotherapy for at least the first 4 hours of sedation
I	High dose Dexmedetomidine (> 1mcg/kg/hr)
C	Standard dose Dexmedetomidine (≤ 1mcg/kg/hr)
O	Percentage of time spent within goal RASS range while on dexmedetomidine

- Retrospective
- Chart review
- Single center
- 2017.11.1 – 2018.12.31

	Standard-dose (n = 121)	High-dose (n = 23)	*P*-value
Highest dose (mcg/kg/h)	0.75 (0.4-1)	1.5 (1.5-1.7)	<.001
Propofol	9 (7.4)	4 (17.4)	
Midazolam	2 (1.7)	1 (4.3)	
Percentage of time spent within goal RASS	84.5 (47-100)	45.5 (30.1-85.4)	.013
Percentage of time below goal RASS range (oversedated)	0 (0-13.5)	11 (0-32)	.019
Percentage of time above goal RASS range (undersedated)	3.2 (0-22)	21.7 (0-34.9)	.028

使用High dose的Dexmedetomidine可能無法增加達到目標RASS的時數且high dose組有更高比例為under sedated而須併用其他sedative

Thanks