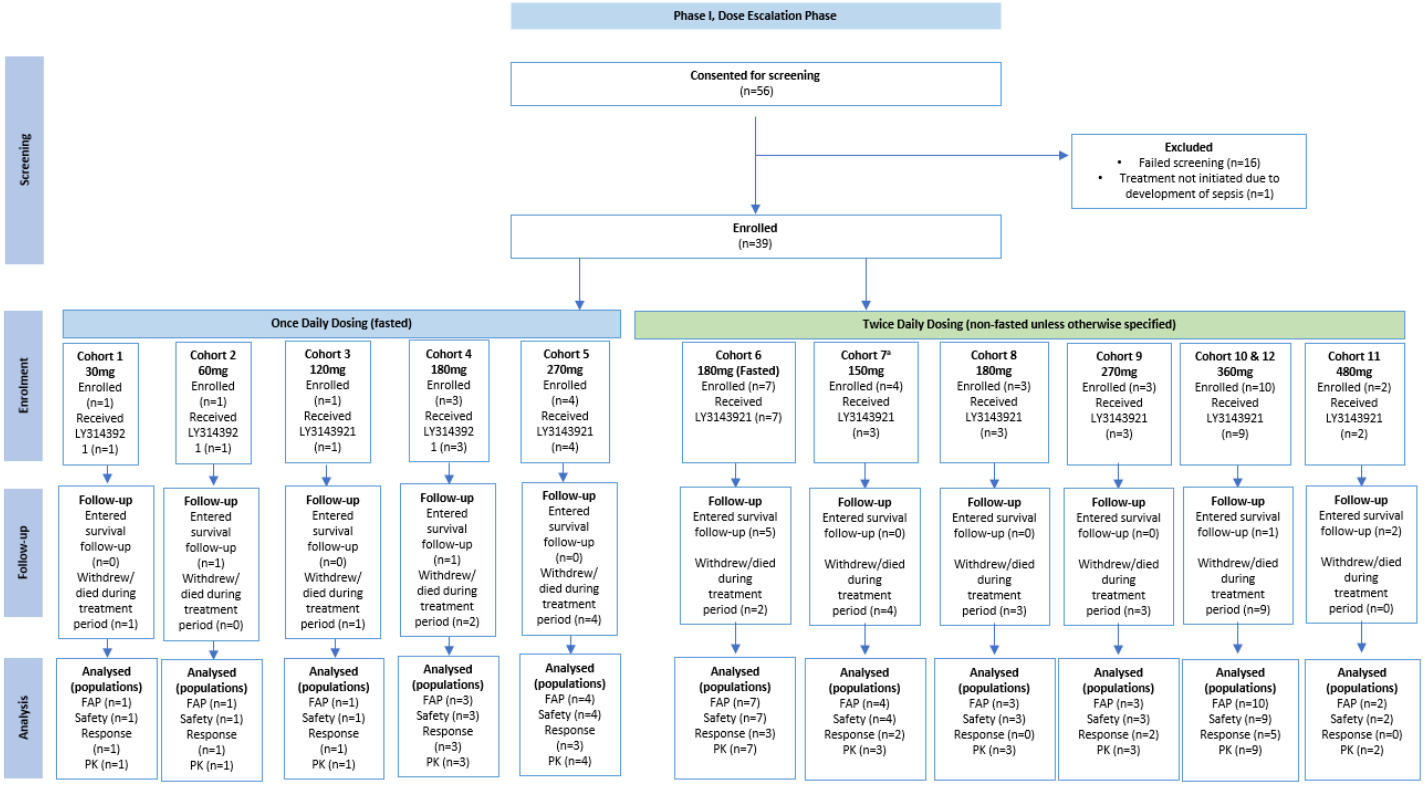
CRUKD/17/004, A Cancer Research UK Phase I Trial of LY3143921 Hydrate (a Cdc7 Inhibitor) Given Orally in Adult Patients with Advanced Solid Tumours Basic Results Summary for ISRCTN

https://doi.org/10.1186/ISRCTN84044406

PARTICIPANT FLOW

Patient Disposition for the Dose Escalation Phase of Trial CRUKD/17/004



Abbreviations: FAP=Full Analysis Population; LY3143921=LY3143921 hydrate; n=number of patients with the characteristic of interest; PK=pharmacokinetic.

[a] In Cohort 7, one patient was withdrawn from the trial due to progressive disease but reported a partial response at a subsequent scan and was re-enrolled with a different patient number. This patient has only been included once in this diagram, but reported as two separate patients in the results tables below and in the Clinical Study Report. The enrolled total for Cohort 7 also includes one patient who was eligible at screening and therefore enrolled onto the trial, but found to be ineligible immediately prior to dosing; therefore, they did not receive LY3143921 hydrate.

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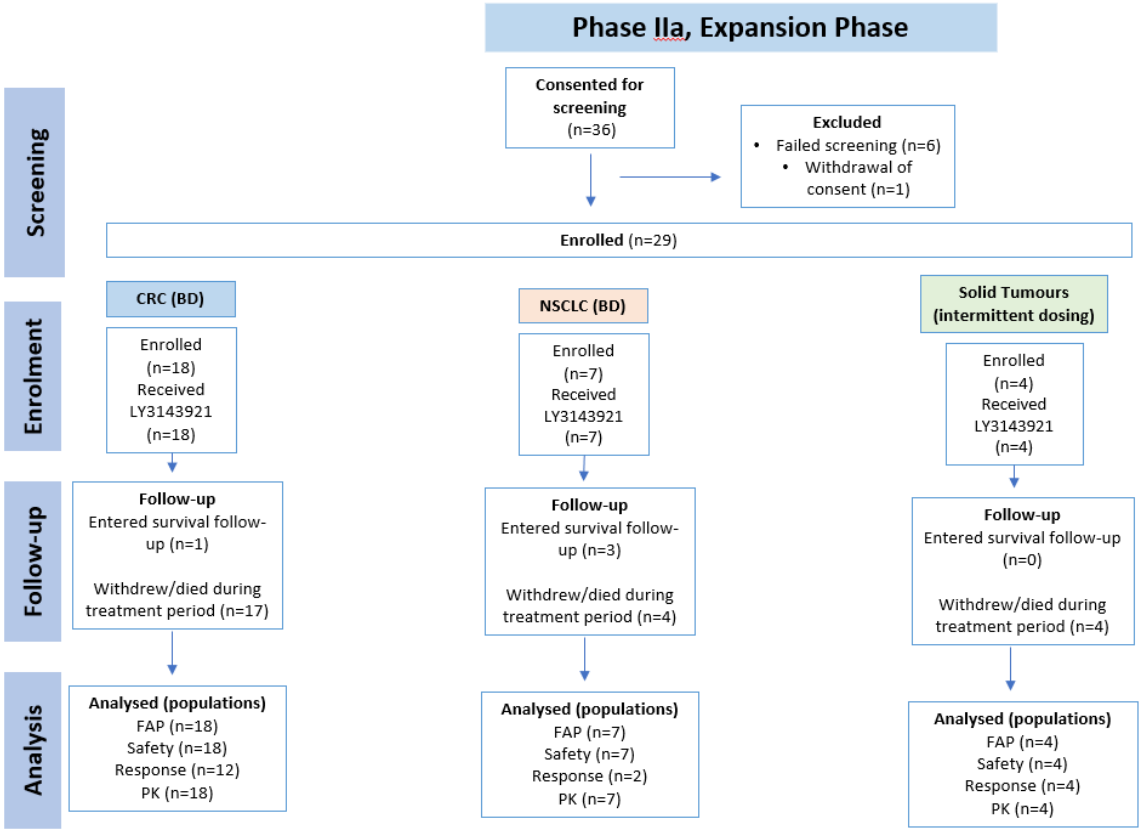
Patient Disposition for the Dose Escalation Phase of Trial CRUKD/17/004



Abbreviations: BD=twice daily dosing (from Cycle 1 Day 1 onwards); CRC=colorectal cancer; FAP=Full Analysis Population; LY3143921=LY3143921 hydrate; n=number of patients with the characteristic of interest; NSCLC=non-small cell lung cancer; PK=pharmacokinetic.

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BASELINE CHARACTERISTICS (FULL ANALYSIS POPULATION)

DOSE ESCALATION PHASE

Baseline Characteristics by Cohort (Dose Escalation Phase, Full Analysis Population)

		Cohort[(a)]										
		OD Dosing					BD Dosing					
Characteristic	All Dose Escalation (N=39)	1 30 mg (N=1)	2 60 mg (N=1)	3 120 mg (N=1)	4 180 mg (N=3)	5 270 mg (N=4)	6 180 mg (N=7)	7 150 mg (N=4)	8 180 mg (N=3)	9 270 mg (N=3)	10 & 12 360 mg (N=10)	11 480 mg (N=2)
Sex (n)												
Female	23	1	1	1	2	1	5	4	2	1	3	2
Male	16	0	0	0	1	3	2	0	1	2	7	0
Age (years)												
Mean	57.1	50	66	59	67.3	68.8	60.3	50	56.7	50.3	54	45.5
Median	57	50	66	59	66	69	62	55	60	49	53.5	45.5
Minimum	33	50	66	59	62	61	52	33	44	49	42	37
Maximum	76	50	66	59	74	76	69	57	66	53	71	54
WHO Performance Status (n)												
0	13	0	1	0	1	2	4	1	0	0	4	0
1	26	1	0	1	2	2	3	3	3	3	6	2

Abbreviations: BD=twice daily (from Cycle 1 Day 1 onwards); N=number of patients in the cohort; n=number of patients with the characteristic of interest; OD=once daily; WHO=World Health Organization.
(a) Cohorts 1–6 received LY3143921 hydrate in a fasted state; one patient in Cohort 6 who remained on treatment switched to non-fasted dosing from Cycle 4 Day 3 onwards. Cohorts 7–11 were non-fasted (patients received LY3143921 hydrate in a non-fasted state at Cycle 1 Day -7. At Cycle 1 Day 1, they received LY3143921 hydrate in a fasted state; all subsequent doses were taken non-fasted).

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EXPANSION PHASE

Baseline Characteristics by Cohort (Dose Expansion Phase, Full Analysis Population)

	All Patients (N=29)	CRC (N=18)	NSCLC (N=7)	Intermittent Dosing (N=4)
Sex (n)				
Female	14	7	3	4
Male	15	11	4	0
Age (years)				
Mean	60.8	58.7	69	56
Median	62	58.5	70	55
Minimum	40	43	60	40
Maximum	82	77	82	74
WHO Performance Status (n)				
0	9	6	2	1
1	20	12	5	3

Abbreviations: CRC=colorectal cancer; N=number of patients in the cohort; n=number of patients with the characteristic of interest; NSCLC=non-small cell lung cancer; WHO=World Health Organization.

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OUTCOME MEASURES

PRIMARY OUTCOME MEASURES

Determination of the maximum tolerated dose: The maximal dose at which no more than 1 patient out of up to 6 patients at the same dose level experiences a highly probably or probably LY3143921 hydrate related dose limiting toxicity and the schedule of administration at which the maximum tolerated dose is established

Summary of Dose Limiting Toxicities (Dose Escalation Phase, Safety Population)

		Cohort[(a)]										
		OD Dosing					BD Dosing					
Characteristic	All Dose Escalation (N=38)	1 30 mg (N=1)	2 60 mg (N=1)	3 120 mg (N=1)	4 180 mg (N=3)	5 270 mg (N=4)	6 180 mg (N=7)	7 150 mg (N=4)	8 180 mg (N=3)	9 270 mg (N=3)	10 & 12 360 mg (N=9)	11 480 mg (N=2)
Number of patients evaluable for DLTs												
	35	1	1	1	3	3	6	3	3	3	9	2
Number of patients with DLT												
	5	0	0	0	0	0	2	0	0	0	1	2

Abbreviations: BD=twice daily (from Cycle 1 Day 1 onwards); DLT=dose limiting toxicity; OD=once daily.
MedDRA v26.0
(a) Cohorts 1–6 received LY3143921 hydrate in a fasted state; one patient in Cohort 6 who remained on treatment switched to non-fasted dosing from Cycle 4 Day 3 onwards. Cohorts 7–11 were non-fasted (patients received LY3143921 hydrate in a non-fasted state at Cycle 1 Day -7. At Cycle 1 Day 1, they received LY3143921 hydrate in a fasted state; all subsequent doses were taken non-fasted).

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Causality and grade of serious adverse events: Number of LY314 hydrate related (possibly, probably or highly probably related) serious adverse events by grade

LY3143921 Hydrate-Related Treatment-Emergent Serious Adverse Events (Dose Escalation Phase, Safety Population)

MedDRA System Organ Class MedDRA Preferred Term	No. of Patients (%)/No. of Events											
		Cohort[a]										
		OD Dosing					BD Dosing					
	Overall (N=38)	1 30 mg (N=1)	2 60 mg (N=1)	3 120 mg (N=1)	4 180 mg (N=3)	5 270 mg (N=4)	6 180 mg Fasted (N=7)	7 150 mg (N=4)	8 180 mg Non-fasted (N=3)	9 270 mg (N=3)	10 & 12 360 mg (N=9)	11 480 mg (N=2)
Overall Total	**6 (15.8) /12**	-	-	-	-	-	**3 (2.9) /6**	-	**1 (33.3) /2**	-	-	**2 (100) /4**
Gastrointestinal Disorders	**5 (13.2) /8**	-	-	-	-	-	**2 (28.6) /4**	-	**1 (33.3) /2**	-	-	**2 (100) /2**
Nausea	3 (7.9) /3	-	-	-	-	-	1 (14.3) /1	-	-	-	-	2 (100) /2
Vomiting	2 (5.2) /2	-	-	-	-	-	2 (28.6) /2	-	-	-	-	-
Diarrhoea	1 (2.6) /1	-	-	-	-	-	-	-	1 (33.3) /1	-	-	-
Constipation	1 (2.6) /1	-	-	-	-	-	1 (14.3) /1	-	-	-	-	-
Rectal haemorrhage	1 (2.6) /1	-	-	-	-	-	-	-	1 (33.3) /1	-	-	-
General Disorders and Administration Site Conditions	**1 (2.6) /1**	-	-	-	-	-	-	-	-	-	-	**1 (50.0) /1**
Fatigue	1 (2.6) /1	-	-	-	-	-	-	-	-	-	-	1 (50.0) /1
Metabolism and Nutrition Disorders	**1 (2.6) /1**	-	-	-	-	-	**1 (14.3) /1**	-	-	-	-	-
Hyponatraemia	1 (2.6) /1	-	-	-	-	-	1 (14.3) /1	-	-	-	-	-

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MedDRA System Organ Class MedDRA Preferred Term	No. of Patients (%)/No. of Events										
		Cohort[a]									
		OD Dosing					BD Dosing				
	Overall (N=38)	1 30 mg (N=1)	2 60 mg (N=1)	3 120 mg (N=1)	4 180 mg (N=3)	5 270 mg (N=4)	6 180 mg Fasted (N=7)	7 150 mg (N=4)	8 180 mg Non-fasted (N=3)	9 270 mg (N=3)	10 & 12 360 mg (N=9)	11 480 mg (N=2)
Nervous System Disorders	**1 (2.6) /1**	**-**	**-**	**-**	**-**	**-**	**-**	**-**	**-**	**-**	**-**	**1 (50.0) /1**
Lethargy	1 (2.6)/1	-	-	-	-	-	-	-	-	-	-	1 (50.0) /1
Renal and Urinary Disorders	**1 (2.6) /1**	**-**	**-**	**-**	**-**	**-**	**1 (14.3) /1**	**-**	**-**	**-**	**-**	**-**
Acute kidney injury	1 (2.6) /1	-	-	-	-		1 (14.3) /1	-	-	-	-	

Abbreviations: AE=adverse event; BD=twice daily (from Cycle 1 Day 1 onwards); MedDRA=Medical Dictionary for Regulatory Activities; No.=number; OD=once daily; SOC=System Organ Class.
Related AEs are those with an AE causality of Possible, Probable or Highly probable.
-=not reported
(a) Cohorts 1–6 received LY3143921 hydrate in a fasted state; one patient in Cohort 6 who remained on treatment switched to non-fasted dosing from Cycle 4 Day 3 onwards. Cohorts 7–11 were non-fasted (patients received LY3143921 hydrate in a non-fasted state at Cycle 1 Day -7. At Cycle 1 Day 1, they received LY3143921 hydrate in a fasted state; all subsequent doses were taken non-fasted).
MedDRA v26.0

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LY3143921 Hydrate-Related Treatment-Emergent Serious Adverse Events (Dose Expansion Phase, Safety Population)

	No. of Patients (%)/No. of Events			
MedDRA System Organ Class MedDRA Preferred Term	All Dose Expansion (N=29)	CRC (N=18)	NSCLC (N=7)	Intermittent Dosing (N=4)
Overall Total	**4 (13.8)/5**	**2 (11.1)/2**	**1 (14.3)/2**	**1 (25.0)/1**
Gastrointestinal Disorders	**1 (3.4)/1**	**1 (14.3)/1**	**-**	**-**
Diarrhoea	1 (3.4)/1	1 (14.3)/1	-	-
General Disorders and Administration Site Conditions	**1 (3.4)/1**	**-**	**1 (14.3)/1**	**-**
Idiosyncratic drug reaction	1 (3.4)/1	-	1 (14.3)/1	-
Infections and Infestations	**1 (3.4)/1**	**-**	**1 (14.3)/1**	**-**
Pneumonia	1 (3.4)/1	-	1 (14.3)/1	-
Renal and Urinary Disorders	**1 (3.4)/1**	**1 (5.6)/1**	**-**	**-**
Acute kidney injury	1 (3.4)/1	1 (5.6)/1	-	-
Vascular Disorders	**1 (3.4)/1**	**-**	**-**	**1 (25.0)/1**
Orthostatic hypotension	1 (3.4)/1	-	-	1 (25.0)/1

Abbreviations: CRC=colorectal cancer; MedDRA=Medical Dictionary for Regulatory Activities; No.=number; NSCLC=non-small cell lung cancer.
Related AEs are those with an AE causality of Possible, Probable or Highly probable.
-=not reported.
MedDRA v26.0

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Causality and grade of non-serious adverse events: Number of LY3143921 hydrate related (possibly, probably or highly probably related) non-serious Adverse Events by grade

LY3143921 Hydrate-Related Treatment-Emergent Non-Serious Adverse Events (Dose Escalation Phase, Safety Population)

MedDRA System Organ Class MedDRA Preferred Term	No. of Patients (%)/No. of Events										
		Cohort[a]									
		OD Dosing					BD Dosing				
	Overall (N=38)	1 30 mg (N=1)	2 60 mg (N=1)	3 120 mg (N=1)	4 180 mg (N=3)	5 270 mg (N=4)	6 180 mg Fasted (N=7)	7 150 mg (N=4)	8 180 mg Non-fasted (N=3)	9 270 mg (N=3)	10 & 12 360 mg (N=9)	11 480 mg (N=2)
Overall Total	**38 (100) /258**	**1 (100)/3**	**1 (100) /5**	**1 (100) /12**	**3 (100) /26**	**4 (100) /16**	**7 (100) /42**	**4 (100) /39**	**3 (100) /31**	**3 (100) /26**	**9 (100) /55**	**2 (100) /15**
Gastrointestinal Disorders	**33 (86.8) /125**	**-**	**1 (100) /3**	**1 (100) /1**	**2 (66.7) /13**	**2 (50.0) /6**	**6 (85.7) /21**	**4 (100) /33**	**3 (100) /9**	**3 (100) /11**	**9 (100) /24**	**2 (100) /4**
Nausea	24 (63.2) /47	-	-	1 (100) /1	1 (33.3) /1	2 (50.0) /2	5 (71.4) /8	4 (100) /18	3 (100) /4	3 (100) /6	5 (55.6) /7	-
Vomiting	20 (52.6) /39	-	-	-	-	2 (50.0) /2	5 (71.4) /7	3 (75.0) /14	3 (100) /3	1 (33.3) /1	4 (44.4) /10	2 (100) /2
Diarrhoea	14 (36.8) /24	-	-	-	2 (66.7) /10	1 (25.0) /1	2 (28.6) /3	-	1 (33.3) /1	1 (33.3) /2	5 (55.6) /5	2 (100) /2
Faeces discoloured	2 (5.3) /2	-	-	-	-	-	-	-	1 (33.3) /1	-	1 (11.1) /1	-
Dyspepsia	2 (5.3) /2	-	1 (100) /1	-	-	-	1 (14.3) /1	-	-	-	-	-
Gastrooesophageal reflux disease	2 (5.3) /3	-	-	-	-	-	1 (14.3) /2	-	-	-	1 (11.1) /1	-
Constipation	2 (5.3) /2	-	1 (100) /1	-	-	-	-	-	-	1 (33.3) /1	-	-
Dysphagia	1 (2.6) /1	-	-	-	-	-	-	-	-	1 (33.3) /1	-	-
Eructation	1 (2.6) /1	-	-	-	-	1 (25.0) /1	-	-	-	-	-	-
Flatulence	1 (2.6) /1	-	1 (100) /1	-	-	-	-	-	-	-	-	-
Rectal haemorrhage	1 (2.6) /1	-	-	-	-	-	-	-	1 (33.3) /1	-	-	-

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MedDRA System Organ Class MedDRA Preferred Term	No. of Patients (%)/No. of Events Overall (N=38)	Cohort[a] OD Dosing 1 30 mg (N=1)	2 60 mg (N=1)	3 120 mg (N=1)	4 180 mg (N=3)	5 270 mg (N=4)	BD Dosing 6 180 mg Fasted (N=7)	7 150 mg (N=4)	8 180 mg Non-fasted (N=3)	9 270 mg (N=3)	10 & 12 360 mg (N=9)	11 480 mg (N=2)
Stomatitis	1 (2.6) /2	-	-	-	1 (33.3) /2	-	-	-	-	-	-	-
Vascular Disorders	**22 (57.9) /43**	**1 (100) /1**	**-**	**1 (100) /9**	**1 (33.3) /2**	**3 (75.0) /5**	**3 (42.9) /5**	**3 (75.0) /3**	**3 (100) /4**	**2 (66.7) /4**	**4 (44.4) /9**	**1 (50.0) /1**
Orthostatic hypotension	19 (50.0) /34	1 (100) /1	-	1 (100) /8	1 (33.3) /1	3 (75.0) /3	2 (28.6) /4	2 (50.0) /2	2 (66.7) /3	2 (66.7) /4	4 (44.4) /7	1 (50.0) /1
Hypotension	6 (15.8) /6	-	-	1 (100) /1		1 (25.0) /1	1 (14.3) /1	1 (25.0) /1	-	-	2 (22.2) /2	-
Hypertension	3 (7.9) /3	-	-	-	1 (33.3) /1	1 (25.0) /1	-	-	1 (33.3) /1	-	-	-
General Disorders and Administration Site Conditions	**16 (42.1) /20**	**-**	**-**	**-**	**1 (33.3) /2**	**2 (50.0) /2**	**2 (28.6) /2**	**1 (25.0) /1**	**2 (66.7) /2**	**2 (66.7) /2**	**5 (55.6) /8**	**1 (50.0) /1**
Fatigue	15 (39.5) /19	-	-	-	1 (33.3) /2	1 (25.0) /1	2 (28.6) /2	1 (25.0) /1	2 (66.7) /2	2 (66.7) /2	5 (55.6) /8	1 (50.0) /1
Gait disturbance	1 (2.6) /1	-	-	-	-	1 (25.0) /1	-	-	-	-	-	-
Nervous System Disorders	**13 (34.2) /22**	**1 (100) /1**	**1 (100) /2**	**1 (100) /1**	**2 (66.7) /3**	**1 (25.0) /1**	**1 (14.3) /2**	**-**	**1 (33.3) /2**	**2 (66.7) /6**	**2 (22.2) /3**	**1 (50.0) /1**
Dizziness	8 (21.1) /10	-	1 (100) /1	1 (100) /1	1 (33.3) /1	1 (25.0) /1	1 (14.3) /1	-	1 (33.3) /1	2 (66.7) /4	-	-
Dysgeusia	4 (10.5) /4	1 (100) /1	-	-	1 (33.3) /1	-	1 (14.3) /1	-	-	-	-	1 (50.0) /1
Taste disorder	4 (10.5) /4	-	1 (100) /1	-	-	-	-	-	1 (33.3) /1	1 (33.3) /1	1 (11.1) /1	-
Lethargy	2 (5.3) /2	-	-	-	-	-	-	-	-	-	1 (11.1) /2	-
Headache	1 (2.6) /1	-	-	-	-	-	-	-	-	1 (33.3) /1	-	-
Tremor	1 (2.6) /1	-	-	-	1 (33.3) /1	-	-	-	-	-	-	-

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Metabolism and Nutrition Disorders	**13 (34.2) /14**	**1 (100) /1**	**-**	**-**	**-**	**-**	**1 (14.3) /1**	**2 (50.0) /2**	**2 (66.7) /2**	**1 (33.3) /1**	**5 (55.6) /5**	**1 (50.0) /2**
Decreased appetite	10 (26.3) /10	1 (100) /1	-	-	-	-	1 (14.3) /1	2 (50.0) /2	2 (66.7) /2	1 (33.3) /1	3 (33.3) /3	-
Hypercalcaemia	1 (2.6) /1	-	-	-	-	-	-	-	-	-	-	1 (50.0) /1
Hypokalaemia	1 (2.6) /1	-	-	-	-	-	-	-	-	-	-	1 (50.0) /1
Hypophosphataemia	1 (2.6) /1	-	-	-	-	-	-	-	-	-	1 (11.1) /1	-
Increased appetite	1 (2.6) /1	-	-	-	-	-	-	-	-	-	1 (11.1) /1	-
Investigations	**8 (21.1) /18**	**-**	**-**	**-**	**1 (33.3) /2**	**2 (50.0) /2**	**1 (14.3) /3**	**-**	**2 (66.7) /8**	**-**	**2 (22.2) /3**	**-**
AST increased	4 (10.5) /5	-	-	-	-	-	-	-	2 (66.7) /3	-	2 (22.2) /2	-
Blood alkaline phosphatase increased	2 (5.3) /2	-	-	-	-	-	-	-	2 (66.7) /2	-	-	-
Blood bilirubin increased	2 (5.3) /2	-	-	-	-	1 (25.0) /1	-	-	1 (33.3) /1	-	-	-
ALT increased	2 (5.3) /2	-	-	-	-	1 (25.0) /1	-	-	1 (33.3) /1	-	-	-
Adjusted calcium increased	1 (2.6) /1	-	-	-	-	-	1 (14.3) /1	-	-	-	-	-
Blood phosphorus decreased	1 (2.6) /1	-	-	-	1 (33.3) /1	-	-	-	-	-	-	-
Blood potassium decreased	1 (2.6) /1	-	-	-	1 (33.3) /1	-	-	-	-	-	-	-
GGT increased	1 (2.6) /1	-	-	-	-	-	-	-	1 (33.3) /1	-	-	-

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Neutrophil count increased	1 (2.6) /1	-	-	-	-	-	1 (14.3) /1	-	-	-	-	-
Prothrombin time prolonged	1 (2.6) /1	-	-	-	-	-	-	-	-	-	1 (11.1) /1-	-
WBC increased	1 (2.6) /1	-	-	-	-	-	1 (14.3) /1	-	-	-	-	-
Skin and Subcutaneous Tissue Disorders	**3 (7.9) /3**	**-**	**-**	**-**	**1 (33.3) /1**	**-**	**1 (14.3) /1**	**-**	**-**	**-**	**1 (11.1) /1**	**-**
Hair texture abnormal	1 (2.6) /1	-	-	-	-	-	-	-	-	-	1 (11.1) /1	-
Nail disorder	1 (2.6) /1	-	-	-	-	-	1 (14.3) /1	-	-	-	-	-
Pruritus	1 (2.6) /1	-	-	-	1 (33.3) /1	-	-	-	-	-	-	-
Blood and Lymphatic System Disorders	**3 (7.9) /4**	**-**	**-**	**1 (100) /1**	**1 (33.3) /1**	**-**	**-**	**-**	**-**	**-**	**1 (11.1) /2**	**-**
Anaemia	2 (5.3) /2	-	-	1 (100) 1	1 (33.3) /1	-	-	-	-	-	-	-
Lymphopenia	1 (2.6) /2	-	-	-	-	-	-	-	-	-	1 (11.1) /2	-
Respiratory, Thoracic and Mediastinal Disorders	**2 (5.3) /2**	**-**	**-**	**-**	**1 (33.3) /1**	**-**	**-**	**-**	**1 (33.3) /1**	**-**	**-**	**-**
Dysphonia	1 (2.6) /1	-	-	-	1 (33.3) /1	-	-	-	-	-	-	-
Hiccups	1 (2.6) /1	-	-	-	-	-	-	-	1 (33.3) /1	-	-	-
Eye Disorders	**2 (5.3) /2**	**-**	**-**	**-**	**1 (33.3) /1**	**-**	**1 (14.3) /1**	**-**	**-**	**-**	**-**	**-**
Lacrimation increased	1 (2.6) /1	-	-	-	1 (33.3) /1	-	-	-	-	-	-	-

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MedDRA System Organ Class MedDRA Preferred Term	No. of Patients (%)/No. of Events Overall (N=38)	Cohort[a] OD Dosing 1 30 mg (N=1)	2 60 mg (N=1)	3 120 mg (N=1)	4 180 mg (N=3)	5 270 mg (N=4)	BD Dosing 6 180 mg Fasted (N=7)	7 150 mg (N=4)	8 180 mg Non-fasted (N=3)	9 270 mg (N=3)	10 & 12 360 mg (N=9)	11 480 mg (N=2)
Vision blurred	1 (2.6) /1	-	-	-	-	-	1 (14.3) /1	-	-	-	-	-
Endocrine Disorders	**1 (2.6) /1**	**-**	**-**	**-**	**-**	**-**	**-**	**-**	**-**	**1 (33.3) /1**	**-**	**-**
Hypothyroidism	1 (2.6) /1	-	-	-	-	-	-	-	-	1 (33.3) /1	-	-
Cardiac Disorders	**1 (2.6) /1**	**-**	**-**	**-**	**-**	**-**	**-**	**-**	**-**	**-**	**-**	**1 (50.0) /1**
Sinus tachycardia	1 (2.6) /1	-	-	-	-	-	-	-	-	-	-	1 (50.0) /1
Musculoskeletal and Connective Tissue Disorders	**1 (2.6) /1**	-	-	-	-	-	-	-	-	**1 (33.3) /1**	**-**	**-**
Myalgia	1 (2.6) /1	-	-	-	-	-	-	-	-	**1 (33.3) /1**	**-**	**-**
Psychiatric Disorders	**1 (2.6) /1**	-	-	-	-	-	-	-	-	-	-	**1 (50.0) /1**
Confusional state	1 (2.6) /1	-	-	-	-	-	-	-	-	-	-	1 (50.0) /1
Ear and Labyrinth Disorders	**1 (2.6) /1**	**-**	**-**	**-**	**-**	**-**	**-**	**-**	**1 (33.3) /1**	-	**-**	**-**
Tinnitus	1 (2.6) /1	-	-	-	-	-	-	-	1 (33.3) /1	-	-	-

Abbreviations: AE=adverse event; ALT=alanine aminotransferase; AST=aspartate aminotransferase; BD=twice daily (from Cycle 1 Day 1 onwards); GGT=gamma-glutamyltransferase; MedDRA=Medical Dictionary for Regulatory Activities; No.=number; OD=once daily; SOC=System Organ Class; WBC=white blood cell count. Related AEs are those with an AE causality of Possible, Probable or Highly probable.
-=not reported
(a) Cohorts 1–6 received LY3143921 hydrate in a fasted state; one patient in Cohort 6 who remained on treatment switched to non-fasted dosing from Cycle 4 Day 3 onwards. Cohorts 7–11 were non-fasted (patients received LY3143921 hydrate in a non-fasted state at Cycle 1 Day -7. At Cycle 1 Day 1, they received LY3143921 hydrate in a fasted state; all subsequent doses were taken non-fasted).
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LY3143921 Hydrate-Related Treatment-Emergent Non-Serious Adverse Events (Dose Expansion Phase, Safety Population)

	No. of Patients (%)/No. of Events			
MedDRA System Organ Class MedDRA Preferred Term	All Dose Expansion (N=29)	CRC (N=18)	NSCLC (N=7)	Intermittent Dosing (N=4)
Overall Total	**28 (96.6)/206**	**18 (100)/123**	**7 (100)/55**	**3 (75.0)/28**
Gastrointestinal Disorders	**25 (86.2)/86**	**16 (88.9)/55**	**6 (85.7)/17**	**3 (75.0)/14**
Nausea	22 (75.9)/39	13 (72.2)/18	6 (85.7)/8	3 (75.0)/13
Diarrhoea	14 (48.3)/16	11 (61.1)/13	3 (42.9)/3	-
Vomiting	10 (34.5)/16	8 (44.4)/14	2 (28.6)/2	-
Faeces discoloured	4 (13.8)/4	3 (16.7)/3	1 (14.3)/1	-
Dyspepsia	3 (10.3)/3	3 (16.7)/3	-	-
Retching	2 (6.9)/2	1 (5.6)/1	1 (14.3)/1	-
Constipation	2 (6.9)/2	-	1 (14.3)/1	1 (25.0)/1
Dry mouth	2 (6.9)/2	1 (5.6)/1	1 (14.3)/1	-
Gastrooesophageal reflux disease	1 (3.4)/1	1 (5.6)/1	-	-
Stomatitis	1 (3.4)/1	1 (5.6)/1	-	-
Vascular Disorders	**17 (58.6)/31**	**9 (50.0)/12**	**6 (85.7)/16**	**2 (50.0)/3**
Orthostatic hypotension	13 (44.8)/23	7 (38.9)/9	4 (57.1)/11	2 (50.0)/3
Hypotension	4 (13.8)/4	2 (11.1)/2	2 (28.6)/2	-
Hypertension	3 (10.3)/4	1 (5.6)/1	2 (28.6)/3	-
General Disorders and Administration Site Conditions	**16 (55.2)/23**	**9 (50.0)/9**	**6 (85.7)/8**	**1 (25.0)/6**
Fatigue	14 (48.3)/19	8 (44.4)/8	5 (71.4)/5	1 (25.0)/6
Pyrexia	2 (6.9)/3	1 (5.6)/1	1 (14.3)/2	-

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MedDRA System Organ Class MedDRA Preferred Term	No. of Patients (%)/No. of Events All Dose Expansion (N=29)	CRC (N=18)	NSCLC (N=7)	Intermittent Dosing (N=4)
Mucosal inflammation	1 (3.4)/1	-	1 (14.3)/1	-
Nervous System Disorders	**13 (44.8)/20**	**7 (38.9)/13**	**4 (57.1)/4**	**2 (50.0)/3**
Lethargy	5 (17.2)/8	5 (27.8)/8	-	-
Taste disorder	4 (13.8)/4	2 (11.1)/2	2 (28.6)/2	-
Dizziness	3 (10.3)/4	1 (5.6)1	1 (5.6)/1	1 (25.0)/2
Migraine	1 (3.4)/2	1 (5.6)/2	-	-
Dysgeusia	1 (3.4)/1	-	1 (14.3)/1	-
Headache	1 (3.4)/1	-	-	1 (25.0)/1
Investigations	**10 (34.5)/18**	**7 (38.9) /13**	**3 (42.9)/5**	**-**
Weight decreased	3 (10.3)/3	3 (16.7)/3	-	-
Aspartate aminotransferase increased	3 (10.3)/3	3 (16.7)/3	-	-
Lymphocyte count decreased	2 (6.9)/2	-	2 (28.6)/2	-
Blood alkaline phosphatase increased	2 (6.9)/2	1 (5.6)/1	1 (14.3)/1	-
Blood bilirubin increased	2 (6.9)/2	1 (5.6)/1	1 (14.3)/1	-
Liver function test abnormal	1 (3.4)/1	1 (5.6)/1	-	-
Adjusted calcium increased	1 (3.4)/1	1 (5.6)/1	-	-
Alanine aminotransferase increased	1 (3.4)/1	1 (5.6)/1	-	-
Blood phosphorus increased	1 (3.4)/1	1 (5.6)/1	-	-
Electrocardiogram abnormal	1 (3.4)/1	-	1 (14.3)/1	-
Blood creatinine increased	1 (3.4)/1	1 (5.6)/1	-	-
Metabolism and Nutrition Disorders	**10 (34.5)/12**	**7 (38.9)/9**	**2 (28.6)/2**	**1 (25.0)/1**
Decreased appetite	7 (24.1)/7	5 (27.8)/5	1 (14.3)/1	1 (25.0)/1

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MedDRA System Organ Class MedDRA Preferred Term	No. of Patients (%)/No. of Events All Dose Expansion (N=29)	CRC (N=18)	NSCLC (N=7)	Intermittent Dosing (N=4)
Hypokalaemia	2 (6.9)/2	2 (11.1)/2	-	-
Hyponatraemia	2 (6.9)/2	1 (5.6)/1	1 (14.3)/1	-
Hypoalbuminaemia	1 (3.4)/1	1 (5.6)/1	-	-
Skin and Subcutaneous Tissue Disorders	**4 (13.8)/6**	**4 (22.2)/6**	**-**	**-**
Madarosis	1 (3.4)/1	1 (5.6)/1	-	-
Rash erythematous	1 (3.4)/1	1 (5.6)/1	-	-
Pruritus	1 (3.4)/1	1 (5.6)/1	-	-
Dry skin	1 (3.4)/1	1 (5.6)/1	-	-
Alopecia	1 (3.4)/1	1 (5.6)/1	-	-
Eczema	1 (3.4)/1	1 (5.6)/1	-	-
Blood and Lymphatic System Disorders	**2 (6.9)/4**	**1 (5.6)/3**	**-**	**1 (25.0)/1**
Lymphopenia	2 (6.9)/2	1 (5.6)/1	-	1 (25.0)1
Neutropenia	1 (3.4)/1	1 (5.6)/1	-	-
Anaemia	1 (3.4)/1	1 (5.6)/1	-	-
Respiratory, Thoracic and Mediastinal Disorders	**2 (6.9)/3**	**1 (5.6)/1**	**1 (14.3)/2**	**-**
Dyspnoea	2 (6.9)/2	1 (5.6)/1	1 (14.3)/1	-
Epistaxis	1 (3.4)/1	-	1 (14.3)/1	-
Eye Disorders	**2 (6.9)/2**	**1 (5.6)/1**	**1 (14.3)/1**	**-**
Visual impairment	1 (3.4)/1	1 (5.6)/1	-	-
Vision blurred	1 (3.4)/1	-	1 (14.3)/1	-

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MedDRA System Organ Class MedDRA Preferred Term	No. of Patients (%)/No. of Events			
	All Dose Expansion (N=29)	CRC (N=18)	NSCLC (N=7)	Intermittent Dosing (N=4)
Cardiac Disorders	**1 (3.4)/1**	**1 (5.6)/1**	**-**	**-**
Palpitations	1 (3.4)/1	1 (5.6)/1	-	-

Abbreviations: CRC=colorectal cancer; MedDRA=Medical Dictionary for Regulatory Activities; No.=number; NSCLC=non-small cell lung cancer.
Related AEs are those with an AE causality of Possible, Probable or Highly probable.
-=not reported.
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SECONDARY OUTCOME MEASURES

Measurement of the pharmacokinetic (PK) parameters maximum observed plasma concentration (C_{max}), time to maximum observed concentration (T_{max}), area under the concentration-time curve from 0 to 24 hours (AUC_{0-24}), half-Life ($T_{1/2}$) volume of distribution (V_z/F) and clearance (CL)

Escalation Phase

Pharmacokinetic Parameters of LY3143921 on Cycle 1 Day -7 and Cycle 1 Day 1 (Dose Escalation Phase, Pharmacokinetic Population)

Cohort[a]	Dose	Cycle Day	C_{max} (ng/mL)	T_{max} (h)	AUC_{0-24} (ng/mL.h)	$T_{1/2}$ (h)	Clearance (L/h)	Vz/F (L)
1 (N=1)	30 mg OD	Cycle 1 Day -7	184	1.2	425	3.35	70.1	NR
2 (N=1)	60 mg OD	Cycle 1 Day -7	175	2.0	502	2.42	119.4	NR
3 (N=1)	120 mg OD	Cycle 1 Day -7	1130	1.0	3138	2.17	38.2	NR
4 (N=3)	180 mg OD	Cycle 1 Day -7	144 – 580	2.0 – 4.0	1716 – 4894	1.9 – 15.3	36.5 – 104.8	NR
5 (N=4)	270 mg OD	Cycle 1 Day -7	474 – 1512	0.5 – 7.9	5124 – 8453	1.9 – 5.8	31.9 – 52.5	NR
6 (N=7)	180 mg BD	Cycle 1 Day -7	384 – 814	0.5 – 4.1	1578 – 3134	1.8 – 5.6	57.2 – 114.0	204 – 592
7 (N=3)[b]	150 mg BD	Cycle 1 Day -7	334 – 632	2.0 – 4.0	1679 – 2569	2.2 – 5.6	58.4 – 88.3	NR
		Cycle 1 Day 1	586 – 928	1.1 – 6.1	2326 – 2522	1.1 - 1.1	59.4 – 64.5	97.2 – 101
8 (N=3)	180 mg BD	Cycle 1 Day -7	492 – 1600	0.9 – 2.0	2178 – 4080	2.3 – 3.7	44.0 – 82.6	217 – 419
		Cycle 1 Day 1	844 – 1644	0.5 – 4.0	2471 – 5260	1.2 – 1.6	34.2 – 72.8	65 – 164
9 (N=3)	270 mg BD	Cycle 1 Day -7	369 – 987	0.55 – 4.0	1966 – 3064	2.7 – 6.0	87.8 – 137.2	NR
		Cycle 1 Day 1[c]	387 – 468	1.0 – 7.0	2815	2.2	95.7	302
10 & 12 (N=9)	360 mg BD	Cycle 1 Day -7	755 – 1930	0.55 – 4.1	2764 – 10060	2.4 – 5.4	35.6 – 130.2	NR
		Cycle 1 Day 1[d]	600 – 2350	0.5 – 2.1	2046 – 10400	1.2 – 4.3	34.6 – 176.1	89.3 – 564
11 (N=2)	480 mg BD	Cycle 1 Day -7	1932 – 2382	4.0 – 10.0	20707 – 21228	3.3 – 3.5	21.6 – 22.2	NR
		Cycle 1 Day 1[d]	1974 – 2550	2.0 – 6.0	23423	3.7	20.4	109

Abbreviations: AUC_{0-24}=area under the plasma concentration-time curve from 0 to 24 hours; BD=twice daily (from Cycle 1 Day 1 onwards); C_{max}=maximum observed plasma concentration; NR=not reported; OD=once daily; PK= pharmacokinetic; $T_{1/2}$=terminal elimination half-life; T_{max}=time to reach C_{max}.
Estimation of $T_{1/2}$ for Day -7 included quantifiable concentrations of LY3143921 measured up to 24 to 72 hours post administration. A minimum of three points in the dose escalation phase were used to calculate $T_{1/2}$.
Estimation of $T_{1/2}$ for Day 1 included quantifiable concentrations of LY3143921 measured up to 8 hours post administration. A minimum of three points were used to calculate $T_{½}$ for all patients except for one patient in Cohort 8 where only two points were used.

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(a) Cohorts 1–6 received LY3143921 hydrate in a fasted state; one patient in Cohort 6 who remained on treatment switched to non-fasted dosing from Cycle 4 Day 3 onwards. Cohorts 7–11 were non-fasted (patients received LY3143921 hydrate in a non-fasted state at Cycle 1 Day -7. At Cycle 1 Day 1, they received LY3143921 hydrate in a fasted state; all subsequent doses were taken non-fasted).
(b) The patient who was withdrawn from the trial and then re-enrolled was excluded from the PK Population at re-enrolment.
(c) It was not possible to calculate multiple PK parameters for two patients with the data available. No data are reported for one additional patient due to the patient vomiting post-drug administration on Day 1 of treatment.
(d) It was not possible to calculate multiple PK parameters for one patient with the data available.

Expansion Phase

Pharmacokinetic Parameters of LY3143921 on Cycle 1 Day 1 (Dose Expansion Phase, Pharmacokinetic Population)

Cohort	Cmax (ng/mL)	Tmax (h)	AUC0-24 (ng/mL.h)	T½ (h)	Clearance (L/h)	Vz/F (L)
CRC (N=18)	352 – 1990	0.5 – 6.0	2063 – 9576	0.8 – 6.3	35.1 – 174	99.4 – 758
NSCLC (N=7)	493 – 1860	0.5 – 4.1	2286 – 7551	1.1 – 8.5	40.3 – 158	141 – 492
Intermittent Dosing (N=4)	795 – 1980	1.1 - 4.0	4007 – 7836	1.4 – 2.6	45.9 – 89.6	90.8 – 339

Abbreviations: AUC0-24=area under the plasma concentration-time curve from 0 to 24 hours; Cmax=maximum observed plasma concentration; CRC=colorectal cancer; NSCLC=non-small cell lung cancer; PK=pharmacokinetic; T½=terminal elimination half-life; Tmax=time to reach Cmax; Vz/F=volume of distribution.
Estimation of T½ for Cycle 1 Day 1 included quantifiable concentrations of LY3143921 measured up to 6 hours post administration. A minimum of two points were used to calculate T½ for all patients.

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Overall Response Rate

Dose Escalation Phase

Overall Response Rate (Dose Escalation Phase, Response Population)

	Cohort[(a)]								
	OD Dosing					BD Dosing			
	1 30 mg (N=1)	2 60 mg (N=1)	3 120 mg (N=1)	4 180 mg (N=3)	5 270 mg (N=3)	6 180 mg (N=3)	7 150 mg (N=2)	9 270 mg (N=2)	10&12 360 mg (N=5)
Overall response rate	0:1	0:1	0:1	0:3	0:3	0:3	0:2	0:2	0:5

Abbreviations: BD=twice daily (from Cycle 1 Day 1 onwards); N=number of patients in the cohort; OD=once daily.
(a) Cohorts 1–6 received LY3143921 hydrate in a fasted state; one patient in Cohort 6 who remained on treatment switched to non-fasted dosing from Cycle 4 Day 3 onwards. Cohorts 7–11 were non-fasted (patients received LY3143921 hydrate in a non-fasted state at Cycle 1 Day -7. At Cycle 1 Day 1, they received LY3143921 hydrate in a fasted state; all subsequent doses were taken non-fasted).

Expansion Phase

Overall Response Rate (Dose Expansion Phase, Response Population

	Cohort		
	CRC (N=12)	NSCLC (N=2)	Intermittent Dosing (N=4)
Overall response rate	0:12	0:2	0:4

Abbreviations: CRC=colorectal cancer; N=number of patients in the cohort; NSCLC=non-small cell lung cancer.

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Median Progression Free Survival

Dose Escalation Phase

Median Progression Free Survival Summary (Dose Escalation Phase, Progression Free Survival Population)

Progression Free Survival (days)	Cohort[(a)]									
	OD Dosing					BD Dosing				
	1 30 mg (N=1)	2 60 mg (N=1)	3 120 mg (N=1)	4 180 mg (N=3)	5 270 mg (N=3)	6 180 mg (N=4)	7 150 mg (N=3)	8 180 mg (N=3)	9 270 mg (N=3)	10&12 360 mg (N=8)
Median	41	227	125	124	47	41	90	41	48	75
Minimum	41	227	125	83	47	40	49	37	43	41
Maximum	41	227	125	195	126	49	127	49	380	136

Abbreviations: BD=twice daily (from Cycle 1 Day 1 onwards); N=number of patients in the cohort; OD=once daily; PFS=progression-free survival.
Summary only includes patients with a PFS event or a follow-up date in the absence of progression. One patient in Cohort 6 (180 mg BD) remained progression-free at the time of analysis, with a censoring timepoint of 2262 days, and was not included.
(a) Cohorts 1–6 received LY3143921 hydrate in a fasted state; one patient in Cohort 6 who remained on treatment switched to non-fasted dosing from Cycle 4 Day 3 onwards. Cohorts 7–11 were non-fasted (patients received LY3143921 hydrate in a non-fasted state at Cycle 1 Day -7. At Cycle 1 Day 1, they received LY3143921 hydrate in a fasted state; all subsequent doses were taken non-fasted).

Expansion Phase

Median Progression Free Survival Summary (Dose Expansion Phase, Progression Free Survival Population)

Progression Free Survival (days)	Cohort		
	CRC (N=17)	NSCLC (N=7)	Intermittent Dosing (N=4)
Median	85	82	36
Minimum	28	14	35
Maximum	194	190	79

Abbreviations: CRC=colorectal cancer; N=number of patients in the cohort; NSCLC=non-small cell lung cancer.

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ADVERSE EVENTS SUMMARIES:

Dose Escalation Phase

Summary of Treatment-Emergent Adverse Events Experienced by ≥2 Patients Overall (Dose Escalation Phase, Safety Population)

MedDRA System Organ Class MedDRA Preferred Term	No. of Patients (%)/No. of events										
		Cohort[a]									
		OD Dosing					BD Dosing				
	Overall (N=38)	1 30 mg (N=1)	2 60 mg (N=1)	3 120 mg (N=1)	4 180 mg (N=3)	5 270 mg (N=4)	6 180 mg (N=7)	7 150 mg (N=4)	8[b] 180 mg (N=3)	9 270 mg (N=3)	10 & 12 360 mg (N=9)	11 480 mg (N=2)
Overall Total	**38 (100) /693**	**1 (100) /17**	**1 (100) /21**	**1 (100) /19**	**3 (100) /64**	**4 (100) /69**	**7 (100) /123**	**4 (100) /126**	**3 (100) /54**	**3 (100) /53**	**9(100) /116**	**2 (100) /31**
Gastrointestinal Disorders	**37 (97.4) /247**	**1 (100) /6**	**1 (100) /6**	**1 (100) /2**	**3 (100) /25**	**3 (75.0) /17**	**7 (100.0) /54**	**4 (100) /56**	**3 (100.0) /16**	**3 (100) /19**	**9 (100) /37**	**2 (100) /9**
Nausea	32 (84.2) /65	1 (100) /5	1 (100) /1	1 (100) /1	2 (66.7) /3	3 (75.0) /4	6 (85.7) /11	4 (100) /19	3 (100.0) /4	3 (100) /6	6 (66.7) /8	2 (100) /3
Vomiting	30 (78.9) /61	1 (100) /1	-	1 (100) /1	3 (100) /3	3 (75.0) /4	6 (85.7) /14	4 (100) /18	3 (100.0) /3	2 (66.7)/3	5 (55.6) /12	2 (100) /2
Diarrhoea	22 (57.9) /39	-	1 (100) /1	-	3 (100) /13	1 (25.0) /1	5 (71.4) /7	2 (50.0) /5	1 (33.3) /1	1 (33.3) /2	6 (66.7) /7	2 (100)/2
Constipation	17 (44.7) /29	-	1 (100) /2	-	1 (33.3) /1	1 (25.0) /2	3 (42.9) /3	4 (100.0) /11	2 (66.7) /5	1 (33.3) /1	4 (44.4) /4	-
Abdominal pain	8 (21.1) /11	-	-	-	1 (33.3) /2	1 (25.0) /2	2 (28.6) /3	-	-	2 (66.7) /2	2 (22.2) /2	-
Dysphagia	4 (10.5) /8	-	-	-	-	-	1 (14.3) /5	-	-	1 (33.3) /1	-	2 (100) /2
Abdominal pain upper	4 (10.5) /7	-	-	-	-	1 (25.0) /2	-	1 (25.0) /3	-	2 (66.7) /2	-	-
Faeces discoloured	4 (10.5) /4	-	-	-	1 (33.3) /1	-	-	-	1 (33.3) /1	1 (33.3) /1	1 (11.1) /1	-

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MedDRA System Organ Class MedDRA Preferred Term	No. of Patients (%)/No. of events										
		Cohort[a]									
		OD Dosing					BD Dosing				
	Overall (N=38)	1 30 mg (N=1)	2 60 mg (N=1)	3 120 mg (N=1)	4 180 mg (N=3)	5 270 mg (N=4)	6 180 mg (N=7)	7 150 mg (N=4)	8[b] 180 mg (N=3)	9 270 mg (N=3)	10 & 12 360 mg (N=9)	11 480 mg (N=2)
Dyspepsia	3 (7.9) /3	-	1 (100)/1	-	-	-	2 (28.6) /2	-	-	-	-	-
Flatulence	2 (5.3) /2	-	1 (100.0) /1	-	-	-	1 (14.3) /1	-	-	-	-	-
Gastrooesophageal reflux disease	2 (5.3) /3	-	-	-	-	-	1 (14.3) /2	-	-	1 (11.1) /1	-	-
Haemorrhoids	2 (5.3) /2	-	-	-	-	-	1 (14.3) /1	-	-	1 (11.1) /1	-	-
Rectal haemorrhage	2 (5.3) /2	-	-	-	-	-	-	-	2 (66.7) /2	-	-	-
General Disorders and Administration Site Conditions	**27 (71.1) /54**	**1 (100) /1**	**1 (100) /1**	**1 (100) /1**	**2 (66.7) /6**	**3 (75.0) /7**	**4 (57.1) /7**	**1 (25.0) /4**	**2 (66.7) /4**	**3 (100) /4**	**7 (77.8) /13**	**2 (100) /6**
Fatigue	21 (55.3) /34	-	1 (100) /1	1 (100) /1	2 (66.7) /5	2 (50.0) /2	3 (42.9) /5	1 (25.0) /2	2 (66.7) /2	2 (66.7) /2	6 (66.7) /11	1 (50.0) /3
Pyrexia	6 (15.8) /6	-	-	-	1 (33.3) /1	2 (50.0) /2	1 (14.3) /1	-	-	1 (33.3) /1	-	1 (50.0) /1
Oedema peripheral	3 (7.9) /4	-	-	-	-	1 (25.0) /1	-	-	1 (33.3) /2	-	-	1 (50.0) /1
Chills	2 (5.3) /2	-	-	-	-	1 (25.0) /1	-	-	-	1 (33.3) /1	-	-
Facial pain	2 (5.3) /2	1 (100.0) 1	-	-	-	-	-	-	-	-	1 (11.1) /1	-
Gait disturbance	2 (5.3) /2	-	-	-	-	1 (25.0) /1	-	1 (25.0) /1	-	-	-	-

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MedDRA System Organ Class MedDRA Preferred Term	No. of Patients (%)/No. of events										
		Cohort[a]									
		OD Dosing					BD Dosing				
	Overall (N=38)	1 30 mg (N=1)	2 60 mg (N=1)	3 120 mg (N=1)	4 180 mg (N=3)	5 270 mg (N=4)	6 180 mg (N=7)	7 150 mg (N=4)	8[b] 180 mg (N=3)	9 270 mg (N=3)	10 & 12 360 mg (N=9)	11 480 mg (N=2)
Non cardiac chest pain	2 (5.3) /2	-	-	-	-	-	1 (14.3) /1	-	-	-	-	1 (50.0) /1
Peripheral swelling	2 (5.3) /2	-	-	-	-	-	-	1 (25.0) /1	-	-	1 (11.1) /1	-
Metabolism and Nutrition Disorders	**27 (71.1) /45**	**1 (100) /1**	**-**	**1 (100) /1**	**3 (100) /5**	**2 (50.0) /3**	**4 (57.1) /8**	**2 (50.0) /7**	**2 (66.7) /2**	**2 (66.7) /2**	**8 (88.9) /12**	**2 (100) /4**
Decreased appetite	19 (50.0) /19	1 (100) /1	-	1 (100) /1	2 (66.7) /2	1 (25.0) /1	2 (28.6) /2	2 (50.0) /2	2 (66.7) /2	2 (66.7) /2	5 (55.6) /5	1 (50.0) /1
Hyponatraemia	4 (10.5) /4	-	-	-	1 (33.3) /1	-	2 (28.6) /2	-	-	-	1 (11.1) /1	-
Hypoalbuminaemia	3 (7.9) /3	-	-	-	1 (33.3) /1	-	1 (14.3) /1	-	-	-	1 (11.1) /1	-
Hypokalaemia	3 (7.9) /7	-	-	-	-	-	-	1 (25.0) /5	-	-	-	2 (100) /2
Hypercalcaemia	2 (5.3) /2	-	-	-	-	-	-	-	-	-	1 (11.1) /1	1 (50.0) /1
Hypomagnesaemia	2 (5.3) /2	-	-	-	1 (33.3) /1	-	1 (14.3) /1	-	-	-	-	-
Hypophosphataemia	3 (7.9) /3	-	-	-	-	-	1 (14.3) /1	-	-	-	2 (22.2) /2	-
Vascular Disorders	**27 (71.1) /57**	**1 (100) /2**	**-**	**1 (100) /9**	**2 (66.7) /3**	**3 (75.0) /8**	**5 (71.4) /9**	**4 (100) /4**	**3 (100.0) /5**	**2 (66.7) /4**	**5 (55.6) /12**	**1 (50.0) /1**
Orthostatic hypotension	22 (57.9) /40	1 (100) /1	-	1 (100) /8	1 (33.3) /1	3 (75.0) /5	4 (57.1) /7	3 (75.0) /3	2 (66.7) /3	2 (66.7) /4	4 (44.4) /7	1 (50.0) /1

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MedDRA System Organ Class MedDRA Preferred Term	No. of Patients (%)/No. of events										
		Cohort[a]									
		OD Dosing					BD Dosing				
	Overall (N=38)	1 30 mg (N=1)	2 60 mg (N=1)	3 120 mg (N=1)	4 180 mg (N=3)	5 270 mg (N=4)	6 180 mg (N=7)	7 150 mg (N=4)	8[b] 180 mg (N=3)	9 270 mg (N=3)	10 & 12 360 mg (N=9)	11 480 mg (N=2)
Hypotension	9 (23.7) /9	1 (100) /1	-	1 (100) /1	-	2 (50.0) /2	2 (28.6) /2	1 (25.0) /1	-	-	2 (22.2) /2	-
Hypertension	7 (18.4) /7	-	-	-	2 (66.7) /2	1 (25.0) /1	-	-	2 (66.7) /2	-	2 (22.2)/2	-
Respiratory, Thoracic and Mediastinal Disorders	**21 (55.3) /40**	**1 (100) /1**	**1 (100) /7**	**1 (100) /1**	**3 (100) /5**	**2 (50.0) /4**	**3 (42.9) /4**	**3 (75.0) /7**	**2 (66.7) /3**	**2 (66.7) /4**	**2 (22.2) /3**	**1 (50.0) /1**
Dyspnoea	11 (28.9) /12	1 (100) /1	1 (100) /2	1 (100) /1	1 (33.3) /1	1 (25.0) /1	2 (28.6) /2	2 (50.0) /2	-	2 (66.7) /2	-	-
Cough	6 (15.8) /6	-	-	-	3 (100) /3	-	-	1 (25.0) /1	-	-	1 (11.1) /1	1 (50.0) /1
Dysphonia	3 (7.9) /3	-	1 (100) /1	-	1 (33.3) /1	1 (25.0) /1	-	-	-	-	-	-
Haemoptysis	3 (7.9) /4	-	1 (100) /1	-	-	-	-	1 (25.0) /2	-	-	1 (11.1) /1	-
Dyspnoea exertional	2 (5.3) /2	-	-	-	-	-	-	-	1 (33.3) /1	1 (33.3) /1	-	-
Oropharyngeal pain	2 (5.3) /2	-	-	-	-	-	1 (14.3) /1	-	-	-	1 (11.1) /1	-
Productive cough	2 (5.3) /3	-	-	-	-	-	-	1 (25.0) /2	-	1 (33.3) /1	-	-
Infections and Infestations	**17 (44.7) /58**	**-**	**1 (100) /2**	**-**	**2 (66.7) /3**	**2 (50.0) /2**	**4 (57.1) /19**	**2 (50.0) /23**	**1 (33.3) /2**	**1 (33.3) /1**	**3 (33.3) /4**	**1 (50.0) /2**
Lower respiratory tract infection	6 (15.8) /8	-	-	-	-	-	1 (14.3) /2	2 (50.0) /3	-	-	2 (22.2) /2	1 (50.0) /1

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MedDRA System Organ Class MedDRA Preferred Term	No. of Patients (%)/No. of events										
		Cohort[a]									
		OD Dosing					BD Dosing				
	Overall (N=38)	1 30 mg (N=1)	2 60 mg (N=1)	3 120 mg (N=1)	4 180 mg (N=3)	5 270 mg (N=4)	6 180 mg (N=7)	7 150 mg (N=4)	8[b] 180 mg (N=3)	9 270 mg (N=3)	10 & 12 360 mg (N=9)	11 480 mg (N=2)
Urinary tract infection	5 (13.2) /25	-	-	-	-	1 (25.0) /1	1 (14.3) /9	2 (50.0) /13	1 (33.3) 2	-	-	-
Infection	3 (7.9) /3	-	-	-	1 (33.3) /1	1 (25.0) /1	-	-	-	1 (33.3) /1	-	-
Upper respiratory tract infection	3 (7.9) /4	-	-	-	-	-	1 (14.3) /1	2 (50.0) /3	-	-	-	-
Oral candidiasis	3 (7.9) /3	-	1 (100) /1	-	-	-	1 (14.3) /1	1 (25.0) /1	-	-	-	-
Pneumonia	2 (5.3) 3	-	-	-	-	-	-	2 (50.0) /3	-	-	-	-
Viral infection	2 (5.3) /2	-	-	-	1 (33.3) /1	-	1 (14.3) /1	-	-	-	-	-
Musculoskeletal and Connective Tissue Disorders	**17 (44.7) /32**	**-**	**1 (100) /3**	**1 (100) /3**	**2 (66.7) /3**	**3 (75.0) /4**	**2 (28.6) /2**	**2 (50.0) /6**	**3 (100.0) /4**	**1 (33.3) /2**	**2 (22.2) /5**	**-**
Musculoskeletal chest pain	5 (13.2) /7	-	-	1 (100.0) /1	-	-	1 (14.3) /1	2 (50.0) /4	1 (33.3) /1	-	-	-
Back pain	5 (13.2) /5	-	-	-	1 (33.3) /1	1 (25.0) /1	-	-	1 (33.3) /1	-	2 (22.2) /2	-
Arthralgia	4 (10.5) /4	-	-	-	1 (33.3) /1	2 (50.0) /2	-	-	-	-	1 (11.1) /1	-
Pain in extremity	4 (10.5) /4	-	-	1 (100) /1	-	1 (25.0) /1	1 (14.3) /1	-	-	-	1 (11.1) /1	-
Flank pain	2 (5.3) /2	-	-	1 (100.0) 1	-	-	-	-	1 (33.3) /1	-	-	-

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MedDRA System Organ Class MedDRA Preferred Term	No. of Patients (%)/No. of events										
		Cohort[a]									
		OD Dosing					BD Dosing				
	Overall (N=38)	1 30 mg (N=1)	2 60 mg (N=1)	3 120 mg (N=1)	4 180 mg (N=3)	5 270 mg (N=4)	6 180 mg (N=7)	7 150 mg (N=4)	8[b] 180 mg (N=3)	9 270 mg (N=3)	10 & 12 360 mg (N=9)	11 480 mg (N=2)
Muscular weakness	2 (5.3) /2	-	1 (100.0) 1	-	-	-	-	-	-	1 (33.3) /1	-	-
Myalgia	2 (5.3) /2	-	1 (100.0) /1	-	-	-	-	-	-	1 (33.3) /1	-	-
Investigations	**17 (44.7) /43**	**-**	**-**	**-**	**1 (33.3) /2**	**2 (50.0) /6**	**3 (42.9) /7**	**2 (50.0) /6**	**3 (100.0) 12**	**1 (33.3) /1**	**4 (44.4) /6**	**1 (50.0) /3**
AST increased	8 (21.1) /10	-	-	-	-	1 (25.0) /1	-	1 (25.0) /2	2 (66.7) /3	1 (33.3) /1	2 (22.2) /2	1 (50.0) /1
Blood ALP increased	5 (13.2) /5	-	-	-	-	-	-	-	3 (100.0) /3	-	2 (22.2) /2	-
ALT increased	5 (13.2) /8	-	-	-	-	1 (25.0) /2	-	1 (25.0) /3	2 (66.7) /2	-	-	1 (50.0) /1
Blood bilirubin increased	3 (7.9) /3	-	-	-	-	1 (25.0) /1	-	-	1 (33.3) /1	-	-	1 (50.0) /1
Weight decreased	3 (7.9) /3	-	-	-	-	-	1 (14.3) /1	1 (25.0) /1	-	-	1 (11.1) /1	-
Neutrophil count increased	2 (5.3) /2	-	-	-	-	-	1 (14.3) /1	-	1 (33.3) /1	-	-	-
WBC count increased	2 (5.3) /2	-	-	-	-	-	1 (14.3) /1	-	1 (33.3) /1	-	-	-
Nervous System Disorders	**16 (42.1) /41**	**1 (100) /3**	**1 (100) /2**	**1 (100) /1**	**2 (66.7) /4**	**1 (25.0) /8**	**1 (14.3) /3**	**1 (25.0) /2**	**1 (33.3) /2**	**2 (66.7) /6**	**3 (33.3) /8**	**2 (100) /2**
Dizziness	9 (23.7) /12	-	1 (100) /1	1 (100) /1	1 (33.3) /1	1 (25.0) /1	1 (14.3) /2	-	1 (33.3) /1	2 (66.7) /4	1 (11.1) /1	-

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MedDRA System Organ Class MedDRA Preferred Term	No. of Patients (%)/No. of events										
		Cohort[a]									
		OD Dosing					BD Dosing				
	Overall (N=38)	1 30 mg (N=1)	2 60 mg (N=1)	3 120 mg (N=1)	4 180 mg (N=3)	5 270 mg (N=4)	6 180 mg (N=7)	7 150 mg (N=4)	8[b] 180 mg (N=3)	9 270 mg (N=3)	10 & 12 360 mg (N=9)	11 480 mg (N=2)
Dysgeusia	5 (13.2) /5	1 (100) /1	-	-	1 (33.3) /1	1 (25.0) /1	1 (14.3) /1	-	-	-	-	1 (50.0) /1
Headache	4 (10.5) /5	1 (100) /1	-	-	-	1 (25.0) /2	-	-	-	1 (33.3) /1	1 (11.1) /1	-
Taste disorder	4 (10.5) /4	-	1 (100) /1	-	-	-	-	-	1 (33.3) /1	1 (33.3) /1	1 (11.1) /1	-
Lethargy	3 (7.9) /4	-	-	-	-	-	-	1 (25.0) /1	-	-	1 (11.1) /2	1 (50.0) /1
Tremor	2 (5.3) /2	-	-	-	1 (33.3) /1	-	-	1 (25.0) /1	-	-	1 (11.1) /1	-
Blood and Lymphatic System Disorders	**13 (34.2) /18**	**-**	**-**	**1 (100) /1**	**1 (33.3) /1**	**2 (50.0) /2**	**-**	**2 (50.0) /2**	**1 (33.3) /1**	**2 (66.7) /3**	**4 (44.4) /8**	**-**
Anaemia	13 (34.2) /14	-	-	1 (100) /1	1 (33.3) /1	2 (50.0) /2	-	2 (50.0) /2	1 (33.3) /1	2 (66.7) /3	4 (44.4) /4	-
Skin and Subcutaneous Tissue Disorders	**8 (21.1) /11**	**-**	**-**	**-**	**2 (66.7) /3**	**1 (25.0) /2**	**2 (28.6) /3**	**-**	**-**	**1 (33.3) /1**	**2 (22.2) /2**	**-**
Dry skin	2 (5.3) /2	-	-	-	1 (33.3) /1	-	-	-	-	-	1 (11.1) /1	-
Pruritus	2 (5.3) /2	-	-	-	1 (33.3) /1	-	-	-	-	1 (33.3) /1	-	-
Injury, Poisoning and Procedural Complications	**7 (18.4) /11**	**-**	**-**	**-**	**-**	**1 (25.0) /1**	**1 (14.3) /1**	**1 (25.0) /4**	**-**	**2 (66.7) /2**	**2 (22.2) /3**	**-**
Fall	3 (7.9) /3	-	-	-	-	-	-	1 (25.0) /1	-	1 (33.3) /1	1 (11.1) /1	-

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MedDRA System Organ Class MedDRA Preferred Term	No. of Patients (%)/No. of events										
		Cohort[a]									
		OD Dosing					BD Dosing				
	Overall (N=38)	1 30 mg (N=1)	2 60 mg (N=1)	3 120 mg (N=1)	4 180 mg (N=3)	5 270 mg (N=4)	6 180 mg (N=7)	7 150 mg (N=4)	8[b] 180 mg (N=3)	9 270 mg (N=3)	10 & 12 360 mg (N=9)	11 480 mg (N=2)
Hepatobiliary Disorders	**5 (13.2) /6**	-	-	-	-	**2 (50.0) /2**	-	-	**1 (33.3) /2**	-	**1 (11.1) /1**	**1 (50.0) /1**
Hepatic pain	3 (7.9) /4	-	-	-	-	-	-	-	1 (33.3) /2	-	1 (11.1) /1	1 (50.0) /1
Eye Disorders	**5 (13.2) /5**	**1 (100.0) /1**	-	-	**1 (33.3) /1**	-	**1 (14.3) /1**	**1 (25.0) /1**	-	**1 (33.3) /1**	-	-
Vision blurred	2 (5.3) /2	1 (100.0) /1	-	-	-	-	1 (14.3) /1	-	-	-	-	-
Psychiatric Disorders	**4 (10.5) /4**	-	-	-	**1 (33.3) /1**	-	**1 (14.3) /1**	-	-	**1 (33.3) /1**	-	**1 (50.0) /1**
Insomnia	2 (5.3) /2	-	-	-	1 (33.3) /1	-	1 (14.3) /1	-	-	-	-	-
Cardiac Disorders	**4 (10.5) /7**	-	-	-	**1 (33.3) /2**	-	**1 (14.3) /2**	**1 (25.0) /2**	-	-	-	**1 (50.0) /1**
Sinus tachycardia	2 (5.3) /3	-	-	-	1 (33.3) /2	-	-	-	-	-	-	1 (50.0) /1
Ear and Labyrinth Disorders	**4 (10.5) /5**	**1 (100.0) /1**	-	-	-	**1 (25.0) /2**	-	-	**1 (33.3) /1**	**1 (33.3) /1**	-	-
Tinnitus	2 (5.3) /2	1 (100.0) /1	-	-	-	-	-	-	1 (33.3) /1	-	-	-
Renal and Urinary Disorders	**3 (7.9) /4**	-	-	-	-	**1 (25.0) /1**	**1 (14.3) /1**	-	-	-	**1 (11.1) /2**	-
Acute kidney injury	2 (5.3) 2	-	-	-	-	-	1 (14.3) /1	-	-	-	1 (11.1) /1	-

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MedDRA System Organ Class MedDRA Preferred Term	No. of Patients (%)/No. of events										
		Cohort[a]									
		OD Dosing					BD Dosing				
		1	2	3	4	5	6	7	8[b]	9	10 & 12	11
	Overall (N=38)	30 mg (N=1)	60 mg (N=1)	120 mg (N=1)	180 mg (N=3)	270 mg (N=4)	180 mg (N=7)	150 mg (N=4)	180 mg (N=3)	270 mg (N=3)	360 mg (N=9)	480 mg (N=2)
Reproductive System and Breast Disorders[b]	2 (5.3) 2	1 (100.0) /1	-	-	-	-	-	1 (25.0) /1	-	-	-	-

Abbreviations: ALT=alanine aminotransferase; ALP=alkaline phosphatase; AST=aspartate aminotransferase; BD=twice daily (from Cycle 1 Day 1 onwards); MedDRA=Medical Dictionary for Regulatory Activities; No.=number; OD=once daily; SOC=system organ class; WBC=white blood cell.
-=not reported
MedDRA v26.0
(a) Cohorts 1–6 received LY3143921 hydrate in a fasted state; one patient in Cohort 6 who remained on treatment switched to non-fasted dosing from Cycle 4 Day 3 onwards. Cohorts 7–11 were non-fasted (patients received LY3143921 hydrate in a non-fasted state at Cycle 1 Day -7. At Cycle 1 Day 1, they received LY3143921 hydrate in a fasted state; all subsequent doses were taken non-fasted).
(b) There were no preferred terms within this SOC that were experienced by ≥2 patients overall; only the SOC reached this criterion.

Summary of TEAEs leading to Discontinuation of LY3143921 Hydrate and/or Withdrawal from Trial (Dose Escalation Phase, Safety Population)

	No. of Patients (%)/No. of Episodes										
	Cohort[a]										
	OD Dosing					BD Dosing					
	1	2	3	4	5	6	7	8	9	10 & 12	11
	30 mg (N=1)	60 mg (N=1)	120 mg (N=1)	180 mg (N=3)	270 mg (N=4)	180 mg (N=7)	150 mg (N=4)	180 mg (N=3)	270 mg (N=3)	360 mg (N=9)	480 mg (N=2)
TEAEs that led to discontinuation of IMP	-	-	-	-	1 (25.0)/1	3 (42.9)/7	-	-	-	2 (22.2)/3	1 (50.0)/2
TEAEs that led to withdrawal from trial	-	-	-	-	-	3 (42.9)/3	-	-	-	1 (11.1)/2	1 (50.0)/2

Abbreviations: BD=twice daily (from Cycle 1 Day 1 onwards); IMP=Investigational Medicinal Product; N=number of patients in the cohort; No.=number; OD=once daily; SOC=system organ class; TEAE=treatment-emergent adverse event.
-=not reported.

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(a) Cohorts 1–6 received LY3143921 hydrate in a fasted state; one patient in Cohort 6 who remained on treatment switched to non-fasted dosing from Cycle 4 Day 3 onwards. Cohorts 7–11 were non-fasted (Patients received LY3143921 hydrate in a non-fasted state at Cycle 1 Day -7. At Cycle 1 Day 1, they received LY3143921 hydrate in a fasted state; all subsequent doses were taken non-fasted).

Frequency of Treatment Emergent Adverse Events leading to Discontinuation of LY3143921 Hydrate (Dose Escalation Phase, Safety Population)

MedDRA System Organ Class MedDRA Preferred Term	No. of Patients (%)/No. of events										
		Cohort[(a)]									
		OD Dosing					BD Dosing				
	All Dose Escalation (N=38)	1 30 mg (N=1)	2 60 mg (N=1)	3 120 mg (N=1)	4 180 mg (N=3)	5 270 mg (N=4)	6 180 mg (N=7)	7 150 mg (N=4)	8 180 mg (N=3)	9 270 mg (N=3)	10 & 12 360 mg (N=9)	11 480 mg (N=2)
Overall Total	**7(18.4) /13**	**-**	**-**	**-**	**-**	**1 (25.0) /1**	**3 (42.9) /7**	**-**	**-**	**-**	**2 (22.2) /3**	**1 (50.0) /2**
Gastrointestinal Disorders	**4 (10.5) /8**	**-**	**-**	**-**	**-**	**-**	**2 (28.6) /5**	**-**	**-**	**-**	**1 (11.1) /2**	**1 (50.0) /1**
Nausea	3 (7.9) /3	-	-	-	-	-	1 (14.3) /1	-	-	-	1 (11.1) /1	1 (50.0) /1-
Vomiting	3 (7.9) /3	-	-	-	-	-	2 (28.6) /2	-	-	-	1 (11.1) /1	
Constipation	1 (2.6) /1	-	-	-	-	-	1 (14.3) /1	-	-	-	-	-
Dysphagia	1 (2.6) /1	-	-	-	-	-	1 (14.3) /1	-	-	-	-	-
Hepatobiliary Disorders	**1 (2.6) /1**	**-**	**-**	**-**	**-**	**1 (25.0) /1**	-	-	-	-	-	-
Hepatic failure	1 (2.6) /1	-	-	-	-	1 (25.0) /1	-	-	-	-	-	-
Metabolism and Nutrition Disorders	**1 (2.6) /1**	**-**	**-**	**-**	**-**	**-**	**1 (14.3) /1**	**-**	**-**	**-**	**-**	**-**

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MedDRA System Organ Class MedDRA Preferred Term	No. of Patients (%)/No. of events										
		Cohort[a]									
		OD Dosing					BD Dosing				
	All Dose Escalation (N=38)	1 30 mg (N=1)	2 60 mg (N=1)	3 120 mg (N=1)	4 180 mg (N=3)	5 270 mg (N=4)	6 180 mg (N=7)	7 150 mg (N=4)	8 180 mg (N=3)	9 270 mg (N=3)	10 & 12 360 mg (N=9)	11 480 mg (N=2)
Hyponatraemia	1 (2.6) /1	-	-	-	-	-	1 (14.3) /1	-	-	-	-	-
Nervous System Disorders	**1 (2.6) /1**	**-**	**-**	**-**	**-**	**-**	**-**	**-**	**-**	**-**	**-**	**1 (50.0) /1**
Lethargy	1 (2.6) /1	-	-	-	-	-	-	-	-	-	-	1 (50.0) /1
Renal and Urinary Disorders	**1 (2.6) /1**	**-**	**-**	**-**	**-**	**-**	**1 (14.3) /1**	**-**	**-**	**-**	**-**	**-**
Acute kidney injury	1 (2.6) /1	-	-	-	-	-	1 (14.3) /1	-	-	-	-	-
Respiratory, Thoracic and Mediastinal Disorders	**1 (2.6) /1**	**-**	**-**	**-**	**-**	**-**	**-**	**-**	**-**	**-**	**1 (11.1) /1**	
Haemoptysis	1 (2.6) /1	-	-	-	-	-	-	-	-		1 (11.1) /1-	

Abbreviations: BD=twice daily (from Cycle 1 Day 1 onwards); MedDRA=Medical Dictionary for Regulatory Activities; No.=number; OD=once daily; SOC=system organ class. -=not reported.
MedDRA v26.0
(a) Cohorts 1–6 received LY3143921 hydrate in a fasted state; one patient in Cohort 6 who remained on treatment switched to non-fasted dosing from Cycle 4 Day 3 onwards. Cohorts 7–11 were non-fasted (patients received LY3143921 hydrate in a non-fasted state at Cycle 1 Day -7. At Cycle 1 Day 1, they received LY3143921 hydrate in a fasted state; all subsequent doses were taken non-fasted).

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Dose Expansion Phase

Summary of Treatment-Emergent Adverse Events Experienced by ≥2 Patients Overall (Dose Expansion Phase, Safety Population)

MedDRA System Organ Class MedDRA Preferred Term	No. of Patients (%)/No. of Events			
	All Dose Expansion (N=29)	CRC (N=18)	NSCLC (N=7)	Intermittent Dosing (N=4)
Overall Total	**29 (100)/440**	**18 (100)/266**	**7 (100)/128**	**4 (100)/46**
Gastrointestinal Disorders	**26 (89.7)/121**	**16 (88.9)/84**	**6 (85.7)/21**	**4 (100)/16**
Nausea	24 (82.8)/41	15 (83.3)/20	6 (85.7)/8	3 (75.0)/13
Diarrhoea	15 (51.7)/20	11 (61.1)/16	3 (42.9)/3	1 (25.0)/1
Vomiting	12 (41.4)/18	10 (55.6)/16	2 (28.6)/2	-
Constipation	10 (34.5)/16	6 (33.3)/12	3 (42.9)/3	1 (25.0)/1
Abdominal pain	5 (17.2)/5	4 (22.2)/4	1 (14.3)/1	-
Faeces discoloured	4 (13.8)/4	3 (16.7)/3	1 (14.3)/1	-
Dry mouth	3 (10.3)/3	2 (11.1)/2	1 (14.3)/1	-
Dyspepsia	3 (10.3)/3	3 (16.7)/3	-	-
Rectal haemorrhage	2 (6.9)/2	1 (5.6)/1	-	1 (25.0)/1
Retching	2 (6.9)/2	1 (5.6)/1	1 (14.3)/1	-
Investigations	**23 (79.3)/58**	**15 (83.3)/34**	**7 (100)/18**	**1 (25.0)/6**
Aspartate aminotransferase increased	8 (27.6)/8	6 (33.3)/6	1 (14.3)/1	1 (25.0)/1
Weight decreased	5 (17.2)/5	4 (22.2)/4	-	1 (25.0)/1
Blood alkaline phosphatase increased	5 (17.2)/5	3 (16.7)/3	-	1 (25.0)/1
Alanine aminotransferase increased	5 (17.2)/5	3 (16.7)/3	1 (14.3)/1	1 (25.0)/1
Neutrophil count increased	4 (13.8)/4	2 (11.1)/2	2 (28.6)/2	-
White blood cell count increased	4 (13.8)/4	2 (11.1)/2	2 (28.6)/2	-
Lymphocyte count decreased	3 (10.3)/4	1 (5.6)/1	2 (28.6)/3	-
Blood bilirubin increased	3 (10.3)/3	1 (5.6)/1	1 (14.3)/1	1 (25.0)/1
Blood creatinine increased	2 (6.9)/2	2 (11.1)/2	-	-
Adjusted calcium increased	2 (6.9)/2	1 (5.6)/1	1 (14.3)/1	-
Prothrombin time prolonged	2 (6.9)/2	1 (5.6)/1	-	1 (25.0)/1
General Disorders and Administration Site Conditions	**22 (75.9)/44**	**13 (72.2)/23**	**7 (100)/14**	**2 (50.0)/7**
Fatigue	17 (58.6)/24	11 (61.1)/13	5 (71.4)/5	1 (25.0)/6
Pyrexia	6 (20.7)/8	5 (27.8)/6	1 (14.3)/2	-
Mucosal inflammation	3 (10.3)/3	1 (5.6)/1	2 (28.6)/2	-
Oedema peripheral	2 (6.9)/3	2 (11.1)/3	-	-
Vascular Disorders	**19 (65.5)/52**	**11 (61.1)/20**	**6 (85.7)/28**	**2 (50.0)/4**
Orthostatic hypotension	16 (55.2)/36	9 (50.0)/16	5 (71.4)/16	2 (50.0)/4

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MedDRA System Organ Class MedDRA Preferred Term	No. of Patients (%)/No. of Events			
	All Dose Expansion (N=29)	CRC (N=18)	NSCLC (N=7)	Intermittent Dosing (N=4)
Hypotension	5 (17.2)/6	3 (16.7)/3	2 (28.6)/3	-
Hypertension	4 (13.8)/10	1 (5.6)/1	3 (42.9)/9	-
Nervous System Disorders	**17 (58.6)/29**	**8 (44.4)/17**	**5 (71.4)/7**	**4 (100)/5**
Lethargy	6 (20.7)/9	5 (27.8)/8	1 (14.3)/1	-
Headache	4 (13.8)/4	1 (5.6)/1	2 (28.6)/2	1 (25.0)/1
Taste disorder	4 (13.8)/4	2 (11.1)/2	2 (28.6)/2	-
Dizziness	3 (10.3)/4	1 (5.6)/1	1 (14.3)/1	1 (25.0)/2
Metabolism and Nutrition Disorders	**16 (55.2)/29**	**11 (61.1)/21**	**4 (57.1)/7**	**1 (25.0)/1**
Decreased appetite	8 (27.6)/9	5 (27.8)/6	2 (28.6)/2	1 (25.0)/1
Hyponatraemia	5 (17.2)/5	3 (16.7)/3	2 (28.6)/2	-
Hypokalaemia	4 (13.8)/4	4 (22.2)/4	-	-
Hypophosphataemia	3 (10.3)/3	2 (11.1)/2	1 (14.3)/1	-
Hypomagnesaemia	2 (6.9)/2	1 (5.6)/1	1 (14.3)/1	-
Infections and Infestations	**14 (48.3)/21**	**9 (50.0)/12**	**4 (57.1)/8**	**1 (25.0)/1**
Urinary tract infection	4 (13.8)/6	2 (11.1)/2	2 (28.6)/3	-
Infection	3 (10.3)/3	2 (11.1)/3	1 (14.3)/1	-
Oral candidiasis	2 (6.9)/2	2 (11.1)/2	-	-
Lower respiratory tract infection	2 (6.9)/2	-	2 (28.6)/2	-
Pneumonia	2 (6.9)/2	-	2 (28.6)/2	-
Respiratory, Thoracic and Mediastinal Disorders	**11 (37.9)/22**	**5 (27.8)/7**	**5 (71.4)/14**	**1 (25.0)/1**
Dyspnoea	6 (20.7)/8	2 (11.1)/3	4 (57.1)/5	-
Wheezing	3 (10.3)/4	-	3 (42.9)/4	-
Rhinorrhoea	2 (6.9)/2	1 (5.6)/1	-	1 (25.0)/1
Productive cough	2 (6.9)/2	1 (5.6)/1	1 (14.3)/1	-
Skin and Subcutaneous Tissue Disorders	**9 (31.0)/14**	**6 (33.3)/11**	**3 (42.9)/3**	**-**
Rash	2 (6.9)/2	-	2 (28.6)/2	-
Blood and Lymphatic System Disorders	**9 (31.0)/14**	**6 (33.3)/9**	**1 (14.3)/1**	**2 (50.0)/4**
Anaemia	5 (17.2)/7	4 (22.2)/5	-	1 (25.0)/2
Neutropenia	3 (10.3)/3	2 (11.1)/2	1 (14.3)/1	-
Thrombocytopenia	2 (6.9)/2	1 (5.6)/1	-	1 (25.0)/1
Lymphopenia	2 (6.9)/2	1 (5.6)/1	-	1 (25.0)/1
Musculoskeletal and Connective Tissue Disorders	**9 (31.0)/12**	**7 (38.9)/9**	**1 (14.3)/2**	**1 (25.0)/1**
Back pain	3 (10.3)/4	1 (5.6)/1	1 (14.3)/2	1 (25.0)/1
Arthralgia	2 (6.9)/2	2 (11.1)/2	-	-
Muscular weakness	2 (6.9)/2	2 (11.1)/2	-	-

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MedDRA System Organ Class MedDRA Preferred Term	No. of Patients (%)/No. of Events			
	All Dose Expansion (N=29)	CRC (N=18)	NSCLC (N=7)	Intermittent Dosing (N=4)
Renal and Urinary Disorders	**5 (17.2)/10**	**4 (22.2)/8**	**1 (14.3)/2**	-
Acute kidney injury	3 (10.3)/3	3 (16.7)/3	-	-
Urinary incontinence	2 (6.9)/2	1 (5.6)/1	1 (14.3)/1	-
Micturition urgency	2 (6.9)/2	1 (5.6)/1	1 (14.3)/1	-
Psychiatric Disorders	**4 (13.8)/5**	**3 (16.7)/4**	**1 (14.3)/1**	-
Depressed mood	2 (6.9)/2	2 (11.1)/2	-	-
Cardiac Disorders	**3 (10.3)/3**	**2 (11.1)/2**	**1 (14.3)/1**	-
Palpitations	2 (6.9)/2	1 (5.6)/1	1 (14.3)/1	-
Injury, Poisoning and Procedural Complications(a)	**2 (6.9)/2**	**2 (11.1)/2**	-	-
Reproductive System and Breast Disorders(a)	**2 (6.9)/2**	**2 (11.1)/2**	-	-
Eye Disorders(a)	**2 (6.9)/2**	**1 (5.6)/1**	**1 (14.3)/1**	-

Abbreviations: CRC=colorectal cancer; MedDRA=Medical Dictionary for Regulatory Activities; No.=number; NSCLC=non-small cell lung cancer.
-=not reported.
MedDRA v26.0
(a) There were no preferred terms within this System Organ Class that were experienced by ≥2 patients Overall; only the System Organ Class reached this criterion.

CRUKD/17/004, A Cancer Research UK Phase I Trial of LY3143921 Hydrate (a Cdc7 Inhibitor) Given Orally in Adult Patients with Advanced Solid Tumours Basic Results Summary for ISRCTN

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Summary of Treatment Emergent Adverse Events leading to Discontinuation of LY3143921 Hydrate and/or Withdrawal from Trial (Dose Expansion Phase, Safety Population)

	No. of Patients/No. of Events		
	CRC (N=18)	NSCLC (N=17)	Intermittent Dosing (N=4)
TEAEs that led to discontinuation of IMP	1 (5.6)/2	1 (14.3)/1	-
TEAEs that led to withdrawal from trial	2 (11.1)/2	1 (14.3)/1	-

Abbreviations: CRC=colorectal cancer; IMP=Investigational Medicinal Product; No.=number; N=number of patients in the cohort; NSCLC=non-small cell lung cancer; TEAE=treatment-emergent adverse event.
-=not reported.

Frequency of Treatment Emergent Adverse Events leading to Discontinuation of LY3143921 Hydrate (Dose Expansion Phase, Safety Population)

MedDRA System Organ Class MedDRA Preferred Term	No. of Patients (%)/No. of Events			
	All Dose Expansion (N=29)	CRC (N=18)	NSCLC (N=7)	Intermittent Dosing (N=4)
Overall Total	**2 (6.9)/3**	**1 (5.6)/2**	**1 (14.3)/1**	**-**
General Disorders and Administration Site Conditions	**1 (3.4)/1**	**-**	**1 (14.3)/1**	**-**
Idiosyncratic drug reaction	1 (3.4)/1	-	1 (14.3)/1	-
Metabolism and Nutrition Disorders	**1 (3.4)/1**	**1 (5.6)/1**	-	-
Hyponatraemia	1 (3.4)/1	1 (5.6)/1	-	-
Renal and Urinary Disorders	**1 (3.4)/1**	**1 (5.6)/1**	-	-
Acute kidney injury	1 (3.4)/1	1 (5.6)/1	-	-

Abbreviations: CRC=colorectal cancer; MedDRA=Medical Dictionary for Regulatory Activities; No.=number; NSCLC=non-small cell lung cancer.
-=not reported.
MedDRA v26.0