The ROYAL MARSDEN
NHS Foundation Trust

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European Medicines Agency

EudraCT registration team

17th December 2021

Dear EudraCT registration desk,

Re: Confirmation of a lack of results for a specific trial

EudraCT reference: 2017000370-10

Protocol title: Avelumab plus fluoropyrimidine-based chemotherapy as adjuvant treatment for stage III dMMR or POLE exonuclease domain mutant colon cancer (POLEM)

The Chief Investigator and the sponsor representative of the above clinical trial would like to notify the MHRA that no results will be uploaded to the EudraCT record because the trial was prematurely ended. This earlier end of the clinical trial is not based on grounds of safety.

The clinical trial was prematurely ended as the funder of the study and IMP supplier, Merck, decided to withdraw support for the study due to slow patient recruitment. The trial is permanently closed to enrolment and all participants have completed all research-related activities. The analysis includes data captured up to the date of the last patient's 28-day safety follow-up which took place on the 5th January 2021.

POLEM is a randomised Phase III trial which aimed to recruit a total of 402 patients. At the time of trial closure, 30 patients had been randomised and treated. Due to the lack of data, the 6-month and 1-year DFS rates were reported instead of the 3-year DFS primary endpoint.

Of the 30 patients, 1 patient in each treatment group relapsed during the 6 months post-randomisation. A total of 4 patients either relapsed or died in the first year following randomisation (1 patient in the control group and 2 patients in the intervention group relapsed, whilst 1 patient in the intervention group died).

The 6-month disease-free survival rate in the ITT population was 93.3 (95% CI: 61.3, 99.0) in the intervention group and 92.9 (95% CI: 59.1, 99.0) in the control group. The 1-year disease-free survival rate in the ITT population was 78.0 (95% CI: 45.5, 92.5) in the intervention group and 92.9 (95% CI: 59.1, 99.0) in the control group.

Four SAEs were observed. Toxicity data are detailed in Appendix 1.

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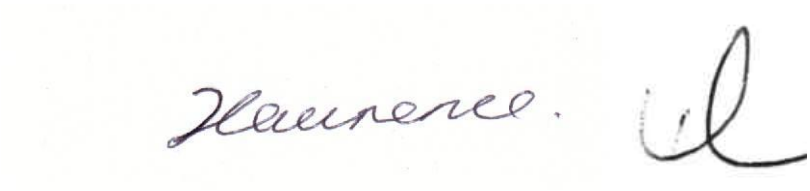
Yours sincerely,



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Appendix 1

Serious Adverse Events

The following table lists details for the four SAEs reported during the trial (Table 1). Three patients in the intervention group (19%) experienced SAEs during avelumab treatment which were reported as probably related to treatment, whilst one patient in the control group (7%) reported an SAE at the end of adjuvant chemotherapy due to COVID-19. All SAEs were either grade 2 or 3 and affected treatment.

Table 1: Serious Adverse Event details

Patient ID	Treatment group	Visit	AE	Grade	Relationship to avelumab treatment	Action to treatment
BM4673001	Intervention	Cycle 10	Pneumonitis	2	Probable	Treatment postponed
RF4673003	Intervention	Cycle 9	Autoimmune Hepatitis	2	Probable	Treatment stopped
RM4673006	Intervention	Cycle 8	Pneumonitis	2	Probable	Treatment interrupted
UC4673002	Control	End of Adjuvant chemo	Covid-19	3	Unrelated	Treatment stopped

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Toxicities

The following table shows the number and proportion of patients who reported an AE under each CTCAE SOC by grade and treatment group (Table 2). For each CTCAE SOC, only the worst grade experienced by each patient is reported.

Table 2: Worst graded AEs reported during the trial, by CTCAE SOC and treatment group

	Intervention (n=16)			Control (n=14)		
	Grade 1	Grade 2	Grade 3	Grade 1	Grade 2	Grade 3
	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
CTCAE SOC						
Blood And Lymphatic System Disorders	4 (25)	0 (0)	0 (0)	2 (14)	0 (0)	0 (0)
Congenital, Familial And Genetic Disorders	0 (0)	0 (0)	0 (0)	1 (7)	0 (0)	0 (0)
Ear And Labyrinth Disorders	1 (6)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Eye Disorders	0 (0)	0 (0)	0 (0)	0 (0)	1 (7)	0 (0)
Gastrointestinal Disorders	8 (50)	2 (13)	0 (0)	7 (50)	3 (21)	1 (7)
General Disorders And Administration Site Conditions	8 (50)	2 (13)	1 (6)	8 (57)	2 (14)	0 (0)
Hepatobiliary Disorders	0 (0)	0 (0)	0 (0)	0 (0)	1 (7)	0 (0)
Immune System Disorders	0 (0)	1 (6)	0 (0)	0 (0)	0 (0)	0 (0)
Infections And Infestations	0 (0)	1 (6)	0 (0)	1 (7)	0 (0)	1 (7)
Injury, Poisoning And Procedural Complications	1 (6)	1 (6)	0 (0)	0 (0)	0 (0)	0 (0)
Investigations	3 (19)	1 (6)	1 (6)	1 (7)	1 (7)	1 (7)
Metabolism And Nutrition Disorders	5 (31)	0 (0)	0 (0)	0 (0)	0 (0)	1 (7)
Musculoskeletal And Connective Tissue Disorders	2 (13)	1 (6)	0 (0)	3 (21)	0 (0)	0 (0)
Neoplasms Benign, Malignant And Unspecified (Incl Cysts And Polyps)	0 (0)	0 (0)	0 (0)	1 (7)	0 (0)	0 (0)
Nervous System Disorders	11 (69)	1 (6)	0 (0)	9 (64)	3 (21)	0 (0)
Psychiatric Disorders	3 (19)	1 (6)	0 (0)	2 (14)	0 (0)	0 (0)
Reproductive System And Breast Disorders	1 (6)	1 (6)	0 (0)	0 (0)	0 (0)	0 (0)
Respiratory, Thoracic And Mediastinal Disorders	5 (31)	2 (13)	0 (0)	1 (7)	0 (0)	1 (7)
Skin And Subcutaneous Tissue Disorders	7 (44)	0 (0)	0 (0)	6 (43)	0 (0)	0 (0)
Vascular Disorders	2 (13)	0 (0)	0 (0)	0 (0)	2 (14)	0 (0)

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The following table shows the number and proportion of patients who reported a grade 3 AE during the trial by CTCAE term (Table 3). Six patients across the trial (20%) experienced a grade 3 (four patients in the control group (29%) and two in the intervention group (13%)). For each CTCAE term, only the worst grade experienced by each patient is reported. No grade 4 or 5 AEs were reported during the trial.

Table 3: CTCAE term listings for Grade 3 AEs reported during the trial by treatment group

	Intervention (n=16)	Control (n=14)	Overall (n=30)
	n (%)	n (%)	n (%)
CTCAE term			
Diarrhoea	0 (0)	1 (7)	1 (3)
GGT Increased	1 (6)	0 (0)	1 (3)
Hypokalaemia	0 (0)	1 (7)	1 (3)
Infections And Infestations - Other	0 (0)	1 (7)	1 (3)
Laryngospasm	0 (0)	1 (7)	1 (3)
Lipase Increased	0 (0)	1 (7)	1 (3)
Pain	1 (6)	0 (0)	1 (3)

The following table lists the CTCAE terms for the three treatment-related AEs reported during the trial, with TRAEs defined as AEs that are either definitely, probably or possibly related to avelumab treatment (Table 4). All three TRAEs were grade 2, reported as probably related to avelumab treatment and were experienced by three different patients in the intervention group.

Table 4: CTCAE term listings for treatment-related AEs reported during the trial

	Intervention (n=16)
	n (%)
CTCAE term	
Pneumonitis	2 (13)
Immune System Disorders - Other*	1 (6)
*Autoimmune hepatitis. All TRAEs were reported as grade 2.	