22nd Jan 2020

Dear Investigator

RE: RAMPART Trial Safety Report to Investigators

Please find enclosed a list of all Serious Adverse Reactions (SARs) and Suspected Unexpected Serious Adverse Reactions (SUSARs) from the RAMPART trial that have occurred between **24/11/2018 and 23/11/2019**. Please note that this is the first Investigator Annual Safety Report as no related events had been reported prior to this period.

The report contains details of 4 SUSARs, including a fatal myasthenia gravis case, and 13 SARs which were reported to the MRC CTU at UCL by the local Investigators. All of the listed events have been clinically reviewed on behalf of the Sponsor by the RAMPART clinical reviewer and Trial Management Group (TMG).

The RAMPART TMG would like to thank you for your continued participation in the trial. Please do not hesitate to contact me if you require any further information.

Kind Regards,

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Listing of all Suspected Unexpected Serious Adverse (drug) Reactions (SUSARs) (24/11/2018 to 23/11/2019)

Case ID / Trial Number / Country / Gender / Age	Reaction	Event Type	Grade	Outcome	Date of onset	Medications	Dose / Route / Formulation	Date of first administration	Date of most recent administration
R0078002C / UK / Male / 51	Musculoskeletal pain	SAR	3	Resolved with sequelae	15-Dec-2018	Durvalumab	1500mg q4w IV	29-Oct-2018	26-Nov-2018
						Tremelimumab	75mg q4w (cycles 1 and 2) IV		
R0116003C / UK / Male / 70	Immune-mediated enterocolitis	SAR	2	Resolved	22-Feb-2019	Durvalumab	1500mg q4w IV	14-Jan-2019	11-Feb-2019
						Tremelimumab	75mg q4w (cycles 1 and 2) IV		
R0512002C / UK / Female / 54	Dyspnoea	SAR	3	Resolved	28-Feb-2019	Durvalumab	1500mg q4w IV	17-Jan-2019	17-Jan-2019
						Tremelimumab	75mg q4w (cycles 1 and 2) IV		
R0116003C / UK / Male / 70	Dyspnoea	SAR	3	Resolved with sequelae	11-Mar-2019	Durvalumab	1500mg q4w IV	14-Jan-2019	11-Feb-2019
						Tremelimumab	75mg q4w (cycles 1 and 2) IV		

R0512002C / UK / Female / 54	Immune-mediated hepatitis	SAR	2	Resolved	11-Apr-2019	Durvalumab	1500mg q4w IV	17-Jan-2019	17-Jan-2019
						Tremelimumab	75mg q4w (cycles 1 and 2) IV		
R0078003B / UK / Male / 53	Pericardial effusion	SUSAR	3	Resolved with sequelae	17-May-2019	Durvalumab	1500mg q4w IV	04-Feb-2019	29-Apr-2019
R0116003C / UK / Male / 70	Exacerbation of COPD	SAR	3	Resolved	31-May-2019	Durvalumab	1500mg q4w IV	14-Jan-2019	11-Feb-2019
						Tremelimumab	75mg q4w (cycles 1 and 2) IV		
R0045004B / UK / Female / 71	Rash maculo-papular	SAR	3	Resolved	18-Jun-2019	Durvalumab	1500mg q4w IV	09-May-2019	06-Jun-2019
R0045004B / UK / Female / 71	Acute kidney injury	SAR	4	Ongoing	27-Aug-2019	Durvalumab	1500mg q4w IV	09-May-2019	31-Jul-2019
R0032006B / UK / Male / 77	Myasthenia Gravis	SUSAR	5	Fatal	31-Jul-2019	Durvalumab	1500mg q4w IV	20-Jun-2019	18-Jul-2019
R0041004B / UK / Male / 75	Colitis	SAR		Ongoing	19-Aug-2019	Durvalumab	1500mg q4w IV	19-Mar-2019	09-Jul-2019
R0054002C / UK / Male / 47	Diarrhoea	SAR	3	Resolved	27-Aug-2019	Durvalumab	1500mg q4w IV	20-Aug-2019	20-Aug-2019
						Tremelimumab	75mg q4w (cycles 1 and 2) IV		
R0078005B / UK /	Guillain-Barre	SUSAR	3	Resolved	16-Sep-	Durvalumab	1500mg q4w	18-Feb-2019	12-Apr-2019

Male / 67	syndrome			with sequelae	2019		IV		
R0075006C / UK / Male / 53	Colitis	SAR	3	Worsened	15-Sep-2019	Durvalumab	1500mg q4w IV	13-Jun-2019	05-Sep-2019
						Tremelimumab	75mg q4w (cycles 1 and 2) IV		
R0047006B / UK / Female / 63	Facial Nerve Disorder	SUSAR	2	Resolved with sequelae	10-Oct-2019	Durvalumab	1500mg q4w IV	20-Sep-2019	20-Sep-2019
R0512006C / UK / Male / 52	Hyperthyroidism	SAR	3	Resolved	21-Oct-2019	Durvalumab	1500mg q4w IV	19-Sep-2019	19-Sep-2019
						Tremelimumab	75mg q4w (cycles 1 and 2) IV		
R0032003C / UK / Male / 48	Diarrhoea	SAR	3	Resolved	17-Nov-2019	Durvalumab	1500mg q4w IV	18-Apr-2019	31-Oct-2019
						Tremelimumab	75mg q4w (cycles 1 and 2) IV		