A summary of model parameters

Table 1. Model input parameters

Variables	Base case value	Sensitivity and scenario analysis		Source
		Lower	Upper	
Model setting				
Discount rate, costs	3.5%	1.5%	5.0%	UK Reference Case
Discount rate, outcomes	3.5%	1.5%	5.0%	UK Reference Case
Time horizon	Lifetime	5,10,15		UK Reference Case
Willingness to pay threshold, £ per QALY gained	£30,000	£20,000		UK ICER Threshold
Patients				
Initial age of patients	54	50	58	Dostarlimab patients
Proportion of males	0.62	0.57	0.67	Dostarlimab patients
Disease free survival				
Excess mortality (SMR) applied to approximate DFS during Dostarlimab course [a]	1.0	1.0	1.2	Assumption, based on no death events in trial
Excess mortality (SMR) applied to approximate DFS after dostarlimab course	12.1	7.8	16.6	Based on validation with medical expert
Excess mortality (SMR) applied to approximate DFS after chemoradiation therapy	20.4	16.6	25.4	Based on internal validation with medical expert
Excess mortality (SMR) applied to approximate DFS after curative surgery	20.4	16.6	25.4	Based on internal validation with medical expert
Health state utilities				

Variables	Base case value	Sensitivity and scenario analysis		Source
		Lower	Upper	
Health state utility while on Dostarlimab course	0.87	0.8	0.9	(Jeong and Cairns, 2016)
Health state utility on chemoradiotherapy	0.87	0.8	0.9	(Jeong and Cairns, 2016)
Health state utility in DFS post dostarlimab	0.87	0.8	0.9	(Jeong and Cairns, 2016)
Health state utility in DFS post chemoradiotherapy course	0.87	0.8	0.9	(Jeong and Cairns, 2016)
HSUV in post ChemoRT surgery	0.84	0.75	0.87	(Jeong and Cairns, 2016)
Health state utility in post-surgery	0.84	0.75	0.87	(Jeong and Cairns, 2016)
Health state utility in DFS post curative surgery	0.87	0.8	0.9	(Jeong and Cairns, 2016)
Health state utility in R/M disease after dostarlimab	0.67	0.6	0.75	(Jeong and Cairns, 2016)
Health state utility in R/M disease after chemoradiation therapy	0.67	0.6	0.75	(Jeong and Cairns, 2016)
Health state utility in R/M disease after surgery	0.67	0.6	0.75	(Jeong and Cairns, 2016)
Health utility norms for UK general population, an age-and sex matched regression equation.	General Population, EQ-5D = 0.9508566 + 0.0212126*male - 0.0002587*age - 0.0000332*age^2			(Ara and Brazier, 2010)
Cost inputs				
Cost of Dostarlimab per cycle	£5887.33			(BNF 2023)
The number of dostarlimab cycles	9			Dostarlimab trial
Disease monitoring in post-dostarlimab DFS, per cycle	£85	£68	£102	Resource use based on (Kennedy, *et al*., 2022), and costs based on UK NHS Reference Costs

Variables	Base case value	Sensitivity and scenario analysis		Source
		Lower	Upper	
Disease monitoring in post-ChemoRT DFS	£85	£68	£102	Assumed the same as above
Disease monitoring in post-surgery DFS	£85	£68	£102	Same as above
Cost of a chemoradiation therapy course	£10,000	£8,000	£12,000	Short-course recommendation from (The Royal College of radiologists, 2019) validated by medical experts and relevant NHS Reference Costs rounded for simplicity
Cost of surgery	£10,000	£8,000	£12,000	Rao (2018) Inflated to 2023 based on PSSRU
Cost per cycle of recurrent/metastatic (R/M) disease after dostarlimab	£1000	£800	£1500	Regimens range from UK cancer research and prices from BNF
Cost per cycle of recurrent/metastatic (R/M) disease after chemoradiotherapy	£1500	£1000	£2000	Assumed 50% higher in patients after chemoradiotherapy, an arbitrary assumption
Cost per cycle of recurrent/metastatic (R/M) disease after surgery	£2000	£1500	£2500	Assumed x2 higher in patients after chemoradiotherapy and surgery
Dostar efficacy (proportion of patients who are disease free at the end of the dostarlimab course)	90%	85%	95%	Based on dostarlimab trial and medical validation
Probability of death during chemoradiotherapy	1%			Assumption >0, for face validity
Efficacy of chemoradiotherapy (% of patients who become disease-free after ChemoRT	33%	25%	40%	Validated with experts

Variables	Base case value	Sensitivity and scenario analysis		Source
		Lower	Upper	
Proportion of patients who are not DFS post ChemoRT, who are eligible for curative intent surgery	0.93	0.9	0.96	Model validation
Curative outcomes of surgery post chemo RT (assumptions)	0.75	0.7	0.8	Model validation exercise
Curative outcomes of surgery post DFS after chemo RT (assumptions)	0.75			Model validation exercise
Perioperative death	0.006	0	0.015	Published economic models, e.g., (Miller, *et al*., 2020) and others
Proportion of patients with stoma after curative intent surgery	0.337	0.25	0.5	(Brown, *et al*., 2014)
Cycle cost of stoma maintenance per cycle (for life)	£74	£60	£89	(Rao, *et al*., 2018)
Reduction of HSUVs in patients with stoma (for life)	3.9%	1.95%	7.82%	(Jeong and Cairns, 2016)

Notes: [a] excess mortality (SMR) applied to age and sex matched general population mortality to simulate DFS.

Summary of assumptions

Due to the initial nature of this health economics assessment, a few structural assumptions were necessary.

Generalizing assumptions were applied, which were subsequently presented and validated by rectal cancer medical experts. These assumptions, along with the model structure, were deemed plausible for addressing the research question. They include:

Patients' pathway

- In the dostarlimab arm, it was assumed that patients, after dostarlimab treatment, would follow a care pathway similar to the standard of care arm. Post-chemoradiation therapy transition probabilities, costs, and outcomes were considered identical to those in the standard of care. While this was accepted as the main assumption in the model, it is worth noting that an HTA model with robust evidence might consider alternative treatment events after ChemoRT in the dostarlimab arm.

Disease-Free survival

- All disease-free states were assumed to be similar, including disease-free survival after chemoradiation therapy, curative surgery, and dostarlimab treatment. In these disease-free states, patients were assumed to have equivalent time to progression, health state utilities, healthcare resource utilization (HCRU), and monitoring costs. Excess mortality was not applied to patients on dostarlimab due to the absence of deaths in the dostarlimab clinical trial.

Recurrent/metastatic disease and non-curative outcomes after surgery

- It was assumed that all model states with recurrent/metastatic (R/M) disease were similar, sharing the same health-related quality of life. Treatment costs were anticipated to increase as patients progressed through the care pathway, with an arbitrary assumption of higher treatment costs in post-chemotherapy R/M and post-surgery R/M scenarios.

Chemoradiation therapy

- Costs and outcomes of chemoradiation therapy were accounted for within a single model cycle. This approach was considered reasonable since the primary outcome of chemo-RT is the proportion of patients achieving disease-free status, with the remaining patients deemed eligible for curative intent surgery (except for a few who were not candidates for surgery).

Surgery

- The surgery step in the treatment pathway was assumed to include all types of surgery, and post-surgery outcomes were represented as either curative (disease-free survival) or non-curative progressed disease. The model did not distinguish between different types of recurrence, as seen in some published models.

Health state utility values (HSUV)

- In the absence of HSUV studies for RC, the model assumed a set of utilities characteristic of a broader CRC.

A summary of model parameters

Table 1. Model input parameters

Variables	Base case value	Sensitivity and scenario analysis		Source
		Lower	Upper	
Model setting				
Discount rate, costs	3.5%	1.5%	5.0%	UK Reference Case
Discount rate, outcomes	3.5%	1.5%	5.0%	UK Reference Case
Time horizon	Lifetime	5,10,15		UK Reference Case
Willingness to pay threshold, £ per QALY gained	£30,000	£20,000		UK ICER Threshold
Patients				
Initial age of patients	54	50	58	Dostarlimab patients
Proportion of males	0.62	0.57	0.67	Dostarlimab patients
Disease free survival				
Excess mortality (SMR) applied to approximate DFS during Dostarlimab course [a]	1.0	1.0	1.2	Assumption, based on no death events in trial
Excess mortality (SMR) applied to approximate DFS after dostarlimab course	12.1	7.8	16.6	Based on validation with medical expert
Excess mortality (SMR) applied to approximate DFS after chemoradiation therapy	20.4	16.6	25.4	Based on internal validation with medical expert
Excess mortality (SMR) applied to approximate DFS after curative surgery	20.4	16.6	25.4	Based on internal validation with medical expert
Health state utilities				

Variables	Base case value	Sensitivity and scenario analysis		Source
		Lower	Upper	
Health state utility while on Dostarlimab course	0.87	0.8	0.9	(Jeong and Cairns, 2016)
Health state utility on chemoradiotherapy	0.87	0.8	0.9	(Jeong and Cairns, 2016)
Health state utility in DFS post dostarlimab	0.87	0.8	0.9	(Jeong and Cairns, 2016)
Health state utility in DFS post chemoradiotherapy course	0.87	0.8	0.9	(Jeong and Cairns, 2016)
HSUV in post ChemoRT surgery	0.84	0.75	0.87	(Jeong and Cairns, 2016)
Health state utility in post-surgery	0.84	0.75	0.87	(Jeong and Cairns, 2016)
Health state utility in DFS post curative surgery	0.87	0.8	0.9	(Jeong and Cairns, 2016)
Health state utility in R/M disease after dostarlimab	0.67	0.6	0.75	(Jeong and Cairns, 2016)
Health state utility in R/M disease after chemoradiation therapy	0.67	0.6	0.75	(Jeong and Cairns, 2016)
Health state utility in R/M disease after surgery	0.67	0.6	0.75	(Jeong and Cairns, 2016)
Health utility norms for UK general population, an age-and sex matched regression equation.	General Population, EQ-5D = 0.9508566 + 0.0212126*male - 0.0002587*age - 0.0000332*age^2			(Ara and Brazier, 2010)
Cost inputs				
Cost of Dostarlimab per cycle	£5887.33			(BNF 2023)
The number of dostarlimab cycles	9			Dostarlimab trial
Disease monitoring in post-dostarlimab DFS, per cycle	£85	£68	£102	Resource use based on (Kennedy, *et al*., 2022), and costs based on UK NHS Reference Costs

Variables	Base case value	Sensitivity and scenario analysis		Source
		Lower	Upper	
Disease monitoring in post-ChemoRT DFS	£85	£68	£102	Assumed the same as above
Disease monitoring in post-surgery DFS	£85	£68	£102	Same as above
Cost of a chemoradiation therapy course	£10,000	£8,000	£12,000	Short-course recommendation from (The Royal College of radiologists, 2019) validated by medical experts and relevant NHS Reference Costs rounded for simplicity
Cost of surgery	£10,000	£8,000	£12,000	Rao (2018) Inflated to 2023 based on PSSRU
Cost per cycle of recurrent/metastatic (R/M) disease after dostarlimab	£1000	£800	£1500	Regimens range from UK cancer research and prices from BNF
Cost per cycle of recurrent/metastatic (R/M) disease after chemoradiotherapy	£1500	£1000	£2000	Assumed 50% higher in patients after chemoradiotherapy, an arbitrary assumption
Cost per cycle of recurrent/metastatic (R/M) disease after surgery	£2000	£1500	£2500	Assumed x2 higher in patients after chemoradiotherapy and surgery
Dostar efficacy (proportion of patients who are disease free at the end of the dostarlimab course)	90%	85%	95%	Based on dostarlimab trial and medical validation
Probability of death during chemoradiotherapy	1%			Assumption >0, for face validity
Efficacy of chemoradiotherapy (% of patients who become disease-free after ChemoRT	33%	25%	40%	Validated with experts

Variables	Base case value	Sensitivity and scenario analysis		Source
		Lower	Upper	
Proportion of patients who are not DFS post ChemoRT, who are eligible for curative intent surgery	0.93	0.9	0.96	Model validation
Curative outcomes of surgery post chemo RT (assumptions)	0.75	0.7	0.8	Model validation exercise
Curative outcomes of surgery post DFS after chemo RT (assumptions)	0.75			Model validation exercise
Perioperative death	0.006	0	0.015	Published economic models, e.g., (Miller, *et al*., 2020) and others
Proportion of patients with stoma after curative intent surgery	0.337	0.25	0.5	(Brown, *et al*., 2014)
Cycle cost of stoma maintenance per cycle (for life)	£74	£60	£89	(Rao, *et al*., 2018)
Reduction of HSUVs in patients with stoma (for life)	3.9%	1.95%	7.82%	(Jeong and Cairns, 2016)

Notes: [a] excess mortality (SMR) applied to age and sex matched general population mortality to simulate DFS.

Summary of assumptions

Due to the initial nature of this health economics assessment, a few structural assumptions were necessary.

Generalizing assumptions were applied, which were subsequently presented and validated by rectal cancer medical experts. These assumptions, along with the model structure, were deemed plausible for addressing the research question. They include:

Patients' pathway

- In the dostarlimab arm, it was assumed that patients, after dostarlimab treatment, would follow a care pathway similar to the standard of care arm. Post-chemoradiation therapy transition probabilities, costs, and outcomes were considered identical to those in the standard of care. While this was accepted as the main assumption in the model, it is worth noting that an HTA model with robust evidence might consider alternative treatment events after ChemoRT in the dostarlimab arm.

Disease-Free survival

- All disease-free states were assumed to be similar, including disease-free survival after chemoradiation therapy, curative surgery, and dostarlimab treatment. In these disease-free states, patients were assumed to have equivalent time to progression, health state utilities, healthcare resource utilization (HCRU), and monitoring costs. Excess mortality was not applied to patients on dostarlimab due to the absence of deaths in the dostarlimab clinical trial.

Recurrent/metastatic disease and non-curative outcomes after surgery

- It was assumed that all model states with recurrent/metastatic (R/M) disease were similar, sharing the same health-related quality of life. Treatment costs were anticipated to increase as patients progressed through the care pathway, with an arbitrary assumption of higher treatment costs in post-chemotherapy R/M and post-surgery R/M scenarios.

Chemoradiation therapy

- Costs and outcomes of chemoradiation therapy were accounted for within a single model cycle. This approach was considered reasonable since the primary outcome of chemo-RT is the proportion of patients achieving disease-free status, with the remaining patients deemed eligible for curative intent surgery (except for a few who were not candidates for surgery).

Surgery

- The surgery step in the treatment pathway was assumed to include all types of surgery, and post-surgery outcomes were represented as either curative (disease-free survival) or non-curative progressed disease. The model did not distinguish between different types of recurrence, as seen in some published models.

Health state utility values (HSUV)

- In the absence of HSUV studies for RC, the model assumed a set of utilities characteristic of a broader CRC.

A summary of model parameters

Table 1. Model input parameters

Variables	Base case value	Sensitivity and scenario analysis		Source
		Lower	Upper	
Model setting				
Discount rate, costs	3.5%	1.5%	5.0%	UK Reference Case
Discount rate, outcomes	3.5%	1.5%	5.0%	UK Reference Case
Time horizon	Lifetime	5,10,15		UK Reference Case
Willingness to pay threshold, £ per QALY gained	£30,000	£20,000		UK ICER Threshold
Patients				
Initial age of patients	54	50	58	Dostarlimab patients
Proportion of males	0.62	0.57	0.67	Dostarlimab patients
Disease free survival				
Excess mortality (SMR) applied to approximate DFS during Dostarlimab course [a]	1.0	1.0	1.2	Assumption, based on no death events in trial
Excess mortality (SMR) applied to approximate DFS after dostarlimab course	12.1	7.8	16.6	Based on validation with medical expert
Excess mortality (SMR) applied to approximate DFS after chemoradiation therapy	20.4	16.6	25.4	Based on internal validation with medical expert
Excess mortality (SMR) applied to approximate DFS after curative surgery	20.4	16.6	25.4	Based on internal validation with medical expert
Health state utilities				

Variables	Base case value	Sensitivity and scenario analysis		Source
		Lower	Upper	
Health state utility while on Dostarlimab course	0.87	0.8	0.9	(Jeong and Cairns, 2016)
Health state utility on chemoradiotherapy	0.87	0.8	0.9	(Jeong and Cairns, 2016)
Health state utility in DFS post dostarlimab	0.87	0.8	0.9	(Jeong and Cairns, 2016)
Health state utility in DFS post chemoradiotherapy course	0.87	0.8	0.9	(Jeong and Cairns, 2016)
HSUV in post ChemoRT surgery	0.84	0.75	0.87	(Jeong and Cairns, 2016)
Health state utility in post-surgery	0.84	0.75	0.87	(Jeong and Cairns, 2016)
Health state utility in DFS post curative surgery	0.87	0.8	0.9	(Jeong and Cairns, 2016)
Health state utility in R/M disease after dostarlimab	0.67	0.6	0.75	(Jeong and Cairns, 2016)
Health state utility in R/M disease after chemoradiation therapy	0.67	0.6	0.75	(Jeong and Cairns, 2016)
Health state utility in R/M disease after surgery	0.67	0.6	0.75	(Jeong and Cairns, 2016)
Health utility norms for UK general population, an age-and sex matched regression equation.	General Population, EQ-5D = 0.9508566 + 0.0212126*male - 0.0002587*age - 0.0000332*age^2			(Ara and Brazier, 2010)
Cost inputs				
Cost of Dostarlimab per cycle	£5887.33			(BNF 2023)
The number of dostarlimab cycles	9			Dostarlimab trial
Disease monitoring in post-dostarlimab DFS, per cycle	£85	£68	£102	Resource use based on (Kennedy, *et al*., 2022), and costs based on UK NHS Reference Costs

Variables	Base case value	Sensitivity and scenario analysis		Source
		Lower	Upper	
Disease monitoring in post-ChemoRT DFS	£85	£68	£102	Assumed the same as above
Disease monitoring in post-surgery DFS	£85	£68	£102	Same as above
Cost of a chemoradiation therapy course	£10,000	£8,000	£12,000	Short-course recommendation from (The Royal College of radiologists, 2019) validated by medical experts and relevant NHS Reference Costs rounded for simplicity
Cost of surgery	£10,000	£8,000	£12,000	Rao (2018) Inflated to 2023 based on PSSRU
Cost per cycle of recurrent/metastatic (R/M) disease after dostarlimab	£1000	£800	£1500	Regimens range from UK cancer research and prices from BNF
Cost per cycle of recurrent/metastatic (R/M) disease after chemoradiotherapy	£1500	£1000	£2000	Assumed 50% higher in patients after chemoradiotherapy, an arbitrary assumption
Cost per cycle of recurrent/metastatic (R/M) disease after surgery	£2000	£1500	£2500	Assumed x2 higher in patients after chemoradiotherapy and surgery
Dostar efficacy (proportion of patients who are disease free at the end of the dostarlimab course)	90%	85%	95%	Based on dostarlimab trial and medical validation
Probability of death during chemoradiotherapy	1%			Assumption >0, for face validity
Efficacy of chemoradiotherapy (% of patients who become disease-free after ChemoRT	33%	25%	40%	Validated with experts

Variables	Base case value	Sensitivity and scenario analysis		Source
		Lower	Upper	
Proportion of patients who are not DFS post ChemoRT, who are eligible for curative intent surgery	0.93	0.9	0.96	Model validation
Curative outcomes of surgery post chemo RT (assumptions)	0.75	0.7	0.8	Model validation exercise
Curative outcomes of surgery post DFS after chemo RT (assumptions)	0.75			Model validation exercise
Perioperative death	0.006	0	0.015	Published economic models, e.g., (Miller, *et al*., 2020) and others
Proportion of patients with stoma after curative intent surgery	0.337	0.25	0.5	(Brown, *et al*., 2014)
Cycle cost of stoma maintenance per cycle (for life)	£74	£60	£89	(Rao, *et al*., 2018)
Reduction of HSUVs in patients with stoma (for life)	3.9%	1.95%	7.82%	(Jeong and Cairns, 2016)

Notes: [a] excess mortality (SMR) applied to age and sex matched general population mortality to simulate DFS.

Summary of assumptions

Due to the initial nature of this health economics assessment, a few structural assumptions were necessary.

Generalizing assumptions were applied, which were subsequently presented and validated by rectal cancer medical experts. These assumptions, along with the model structure, were deemed plausible for addressing the research question. They include:

Patients' pathway

- In the dostarlimab arm, it was assumed that patients, after dostarlimab treatment, would follow a care pathway similar to the standard of care arm. Post-chemoradiation therapy transition probabilities, costs, and outcomes were considered identical to those in the standard of care. While this was accepted as the main assumption in the model, it is worth noting that an HTA model with robust evidence might consider alternative treatment events after ChemoRT in the dostarlimab arm.

Disease-Free survival

- All disease-free states were assumed to be similar, including disease-free survival after chemoradiation therapy, curative surgery, and dostarlimab treatment. In these disease-free states, patients were assumed to have equivalent time to progression, health state utilities, healthcare resource utilization (HCRU), and monitoring costs. Excess mortality was not applied to patients on dostarlimab due to the absence of deaths in the dostarlimab clinical trial.

Recurrent/metastatic disease and non-curative outcomes after surgery

- It was assumed that all model states with recurrent/metastatic (R/M) disease were similar, sharing the same health-related quality of life. Treatment costs were anticipated to increase as patients progressed through the care pathway, with an arbitrary assumption of higher treatment costs in post-chemotherapy R/M and post-surgery R/M scenarios.

Chemoradiation therapy

- Costs and outcomes of chemoradiation therapy were accounted for within a single model cycle. This approach was considered reasonable since the primary outcome of chemo-RT is the proportion of patients achieving disease-free status, with the remaining patients deemed eligible for curative intent surgery (except for a few who were not candidates for surgery).

Surgery

- The surgery step in the treatment pathway was assumed to include all types of surgery, and post-surgery outcomes were represented as either curative (disease-free survival) or non-curative progressed disease. The model did not distinguish between different types of recurrence, as seen in some published models.

Health state utility values (HSUV)

- In the absence of HSUV studies for RC, the model assumed a set of utilities characteristic of a broader CRC.