

Supplementary Table 1: Grading of Prespecified Adverse Events Attributable to Fluoropyrimidines

CTCAE ¹ Term	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5
Neutropenia	-	-	ANC 1,000-500/ μ L; ANC < 1000/ μ L with a single temperature of >38.3 degrees C (101 degrees F) or a sustained temperature of \geq 38 degrees C (100.4 degrees F) for more than one hours	ANC < 500/ μ L; Life threatening consequences; urgent intervention indicated	Death
Diarrhea	Increase of <4 stools per day over baseline; mild increase in ostomy output compared to baseline	Increase of 4-6 stools per day over baseline; moderate increase in ostomy output compared to baseline; limiting instrumental ADL	Increase of \geq 7 stools per day over baseline; hospitalization indicated; severe increase in ostomy output compared to baseline; limiting self-care ADL	Life threatening consequences, urgent intervention indicated	Death
Hand-Foot Syndrome	Rash covering < 10% BSA with or without symptoms (e.g. pruritis, burning, tightness)	Rash covering 10-30% BSA with or without symptoms (e.g. pruritis, burning, tightness); limiting instrumental ADL; rash covering > 30% BSA with or without mild symptoms	Rash covering >30% BSA with moderate or severe symptoms; limiting self-care ADL	Life threatening consequences; rash covering any % BSA, which may or may not be associated with symptoms of pruritis or tenderness and are associated with extensive superinfection with IV antibiotics indicated	Death
Mucositis	Asymptomatic or mild symptoms; intervention not indicated	Moderate pain or ulcer that does not interfere with oral intake; modified diet indicated	Severe pain; interfering with oral intake	Life-threatening consequences; urgent intervention indicated	Death

¹Table abstracted from Common Terminology Criteria for Adverse Events (CTCAE) v.5.0, without modification. https://ctep.cancer.gov/protocoldevelopment/electronic_applications/docs/CTCAE_v5_Quick_Reference_5x7.pdf

Supplementary Table 2: Grading of Prespecified Adverse Events Attributable to Irinotecan

CTCAE ¹ Term	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5
Neutropenia	-	-	ANC 1,000-500/ μ L; ANC < 1000/ μ L with a single temperature of >38.3 degrees C (101 degrees F) or a sustained temperature of \geq 38 degrees C (100.4 degrees F) for more than one hours	ANC < 500/ μ L; Life threatening consequences; urgent intervention indicated	Death
Diarrhea	Increase of <4 stools per day over baseline; mild increase in ostomy output compared to baseline	Increase of 4-6 stools per day over baseline; moderate increase in ostomy output compared to baseline; limiting instrumental ADL	Increase of \geq 7 stools per day over baseline; hospitalization indicated; severe increase in ostomy output compared to baseline; limiting self care ADL	Life threatening consequences, urgent intervention indicated	Death

¹Table abstracted from Common Terminology Criteria for Adverse Events (CTCAE) v.5.0, without modification. https://ctep.cancer.gov/protocoldevelopment/electronic_applications/docs/CTCAE_v5_Quick_Reference_5x7.pdf