Systemic Anti Cancer Treatment Protocol

Lonsurf®
(trifluridine and tipiracil)

PROTOCOL REF: MPHACOLTRI
(Version No: 2.0)

Approved for use in:

Lonsurf (trifluridine–tipiracil) is recommended within its marketing authorisation, as an option for treating metastatic colorectal cancer that has failed at least two prior regimens for advanced/metastatic disease.

Prior regimens could be fluoropyrimidine-, oxaliplatin- or irinotecan-based chemotherapies, anti-vascular endothelial growth factor (VEGF) agents and anti-epidermal growth factor receptor (EGFR) agents. Patients relapsing during or within 6 months of completing adjuvant chemotherapy can count the adjuvant line as one line of therapy for advanced/metastatic disease.

PS 0 – 1

Requires blue-teq registration for funding by NHS England.

Dosage: Day 1 to be Monday

Drug	Route	Dosage
Lonsurf	PO	Days 1 through 5: **35mg/m^2 twice daily** Days 6 through 7: recovery Days 8 through 12: **35mg/m^2 twice daily** Day 13 through 28: recovery

Supportive treatments:

Domperidone 10mg oral tablets, up to 3 times a day or as required

Loperamide 2mg when required

Administration:

Day	Drug	Route	Dose
1 to 5	**Lonsurf**	**PO**	**35mg/m^2 twice daily after food**
6 to 7	Recovery	No treatment	
8 to 12	**Lonsurf**	**PO**	**35mg/m^2 twice daily after food**
13 to 28	Recovery	No treatment	

Tablets to be taken within one hour after breakfast and evening meal.

Number of Lonsurf tablets per dose				
Lonsurf	BSA m^2	Dose in mg twice daily	Tablets per dose	
			15mg	20mg
35mg/m^2	<1.07	35	1	1
	1.07 – 1.22	40	0	2
	1.23 – 1.37	45	3	0
	1.38 – 1.52	50	2	1
	1.53 – 1.68	55	1	2
	1.69 – 1.83	60	0	3
	1.84 – 1.98	65	3	1
	1.99 – 2.14	70	2	2
	2.15 – 2.29	75	1	3
	≥2.30	80	0	4

Main Toxicities:

Lonsurf	
Haematological	Neutropenia, thrombocytopenia, anaemia
Gastrointestinal	Stomatitis, reflux nausea vomiting, constipation, diarrhea, abdominal pain, Rare reactions <3% of patients - colitis, bowel obstruction haemorrhage
Cardiotoxicity	Rare reaction <3% of patients - Myocardial ischaemia, chest

	pain, bradycardia, tachycardia,
Hepatotoxicity	Elevated liver enzymes, Hepatic failure, jaundice
Renal toxicity	Acute renal failure, hematuria
General disorders	Fatigue, myalgia

Investigations:

	Pre	Cycle 1	Cycle 2	Cycle 3	Cycle 4	Ongoing
Clinical assessment	X			X		Every cycle
SACT Assessment	X	X	X	X	X	Every cycle
FBC	X	X	X	X	X	Every cycle
U&E & LFTs	X	X	X	X	X	Every cycle
Informed Consent	X					Verbal each cycle
Weight recorded	X	X	X	X	X	Every cycle

Dose Modifications and Toxicity Management:

For intolerable grade 2 or any toxicity or above grade 3, treatment should be withheld until toxicity resolves to grade 1 or 0. Treatment may then be restarted at a reduced dose level. Treatment may be held for up to 28 days. **If toxicities fail to resolve within 28 days treatment should be permanently discontinued**. Maximum 3 dose reductions permitted. Dose escalation at any time is not recommended.

Haematological toxicity

Unless different limits have been previously agreed by a consultant on an individual basis, proceed on day 1 if:-

ANC ≥ 1.5 x 10^9/L	Platelets ≥ 100 x 10^9/L

For haematological toxicities treatment may be restarted at a reduced dose level when counts recover.

Dose modifications

Level 1 dose reduction: Number of Lonsurf tablets per dose				
Lonsurf	BSA m^2	Dose in mg twice daily	Tablets per dose	
			15mg	20mg
30mg/m^2	<1.09	30	2	0
	1.09 – 1.24	35	1	1
	1.25 – 1.39	40	0	2
	1.40 – 1.54	45	3	0
	1.55 – 1.69	50	2	1
	1.70 – 1.94	55	1	2
	1.95 – 2.09	60	0	3
	2.10 – 2.28	65	3	1
	≥2. 29	70	2	2

Level 2 dose reduction: Number of Lonsurf tablets per dose				
Lonsurf	BSA m^2	Dose in mg twice daily	Tablets per dose	
			15mg	20mg
25mg/m^2	<1.10	25	2	0
	1.10 – 1.29	30	1	1
	1.30 – 1.49	35	0	2
	1.50 – 1.69	40	3	0
	1.70 – 1.89	45	2	1
	1.90 – 2.09	50	1	2
	1.90 – 2.09	55	0	3
	2.10 – 2.29	60	3	1
	≥2. 29		2	2

Level 3 dose reduction number of Lonsurf tablets per dose				
Lonsurf	BSA m^2	Dose in mg twice daily	Tablets per dose	
			15mg	20mg
20mg/m^2	<1.14	20	0	1
	1.14 – 1.34	25	2	1
	1.35 – 1.59	30	2	0
	1.60 – 1.94	35	1	1
	1.95 – 2.09	40	0	2
	2.10 – 2.34	45	3	0
	≥2. 35	50	2	1

Renal Impairment

Not recommended in patients with creatinine clearance below 30mL/min

Hepatic impairment

Not recommended in patients with moderate/severe hepatic impairment

References:

National Institute for Health and Care Excellence (NICE). Trifluridine–tipiracil (Lonsurf) for previously treated metastatic colorectal cancer in adult [TA405] https://www.nice.org.uk/guidance/TA40 , accessed 30 October 2018)

Electronic Medicines Compendium. Summary of product characteristics for trifluridine–tipiracil, https://www.medicines.org.uk/emc/product/7309 (accessed 30 October 2018)

Mayer RJ, Van Cutsem E, Falcone A, Yoshino T, Garcia-Carbonero R, Mizunuma N, et al. Randomized trial of TAS-102 for refractory metastatic colorectal cancer. N Engl J Med 2015; 372(20):1909-19.