Somerset, Wiltshire, Avon and Gloucestershire Cancer Alliance

Ribociclib (Breast) – LOCALLY ADVANCED/METASTATIC

Please note this protocol has been produced in a new format that is currently being piloted. Any feedback on this new format should be sent to SSGMeetings@uhbw.nhs.uk

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Indication

In combination with an aromatase inhibitor for previously untreated, hormone receptor-positive, HER2-negative, locally advanced or metastatic breast cancer.
(NICE TA496)

Phase 3 MONALEESA-2 trial

- Ribociclib plus letrozole (n=334) vs. placebo plus letrozole alone (n=334)
- 18 month PFS: 63% vs 42.2%
- Median OS: 63.9 months vs 51.4 months

In combination with fulvestrant for treating hormone receptor-positive, HER2-negative advanced breast cancer after endocrine therapy, when exemestane plus everolimus is the most appropriate alternative to a CDK4/6 inhibitor
(NICE TA687)

Phase 3 MONALEESA-3 trial

- 2nd line treatment subgroup: Ribociclib plus fulvestrant (n=237) vs placebo plus fulvestrant (n=109)
- Median OS: 40.2 months vs 32.5 months

Regimen details

Advanced/Metastatic

Day	Drug	Dose	Route
1-21 (followed by a 7 day break)	Ribociclib	600mg OD	Oral

Cycle frequency
28 days
Ribociclib is taken for 21 days followed by a 7 day break.

Number of cycles
Until disease progression or unacceptable toxicity.

Pre-medication
Nil

Supportive medication
Nil

Emetogenicity
This regimen has low emetic potential – refer to local policy

Administration
Ribociclib is available as 200mg film-coated tablets. The tablets should be swallowed whole and not chewed, crushed or split prior to swallowing. They may be taken with or without food. Patients should take doses at approximately the same time each day, preferably in the morning. If the patient vomits after taking the dose or misses a dose, an additional dose should not be taken that day and the next prescribed dose should be taken at the usual time.

Grapefruit and grapefruit juice should be **avoided** whilst taking ribociclib. See below for recommended dose reductions when concomitant treatment with ribociclib and strong CYP3A4 inhibitor is unavoidable.

Mandatory investigations – pre first cycle

Investigation	Validity period
FBC	14 days
U&Es* (including creatinine)	14 days
LFTs	14 days
Calcium*	14 days
Phosphate*	14 days
Magnesium*	14 days
ECG (for QTc interval)*	14 days

*QTc should be <450msec to initiate treatment. Any electrolyte abnormalities should also be corrected prior to initiating treatment.

Investigations – pre subsequent cycles

Investigation	Validity period
FBC	2 weekly for first 2 cycles then prior to each cycle
U&Es (including creatinine)	2 weekly for first 2 cycles then prior to each cycle
LFTs	2 weekly for first 2 cycles then prior to each cycle
Calcium	Prior to each cycle for #2-6 then as clinically indicated
Phosphate	Prior to each cycle for #2-6 then as clinically indicated
Magnesium	Prior to each cycle for #2-6 then as clinically indicated
ECG (for QTc interval)	Day 14 of cycle 1 then as clinically indicated

Standard limits for administration to go ahead

If blood results not within range, authorisation to administer must be given by prescriber/ consultant

Investigation	Limit
Neutrophils	≥ 1.0 x 10^9/L
Platelets	≥ 75 x 10^9/L
Creatinine clearance (CrCl)	≥ 30mL/min
Bilirubin	< 2 x ULN
AST/ALT	< 3 x ULN
QTc interval	≤ 480msec

Dose modifications

Dose level	Advanced/Metastatic disease
Starting dose	600mg OD
First dose reduction	400mg OD
Second dose reduction	200mg OD

If 200mg OD is not tolerated, treatment should be discontinued.

Haematological toxicity

Neutrophil count		Platelet count	Action
0.5-1.0 x 10^9/L	or	25-75 x 10^9/L	Hold ribociclib until count recovery. Restart ribociclib at same dose level. If toxicity recurs, hold until recovery then reduce dose by 1 dose level
<0.5 x 10^9/L or febrile neutropenia	or	< 25 x 10^9/L	Hold ribociclib until count recovery Restart ribociclib with 1 dose level reduction

Renal impairment

Creatinine clearance (CrCl)	Dose
≥ 30 ml/min	No dose adjustment required
< 30ml/min	A starting dose of 200mg daily is recommended

Hepatic impairment

Child-Pugh classification	Dose
Class A	No dose adjustment required
Class B or C	A starting dose of 400mg daily is recommended

See below for management of hepatotoxicity emergent on treatment.

Other toxicities

Hepatotoxicity

ALT/AST		Bilirubin	Action
< 3 x ULN	AND	< 2 x ULN	No dose adjustment required
3 – 5 x ULN (if baseline < 3 x ULN)			Withhold ribociclib until returns to baseline then restart at same dose level. If toxicity recurs, resume ribociclib at next lower dose level
3 – 5 x ULN (if baseline > 3 x ULN)			No dose adjustment required
5 – 20 x ULN			Withhold ribociclib until returns to baseline, then restart at next lower dose level If toxicity recurs, discontinue ribociclib
> 20 x ULN			Discontinue ribociclib
> 3 x ULN	AND	> 2 x ULN (in the absence of cholestasis)	Discontinue ribociclib

QT Prolongation

QTcF	Action – Advanced/metastatic breast cancer
>480msec and ≤500msec	Withhold ribociclib If QTcF prolongation resolves to <481 msec, resume treatment at next lower dose level If QTcF >480 msec recurs, withhold until resolves to <481msec, then resume ribociclib at next lower dose level
>500msec	Withhold ribociclib If QTcF prolongation resolves to <481 msec, resume treatment at next lower dose level If QTcF >500msec recurs or QTcF interval prolongation to greater than 500 msec or greater than 60 msec change from baseline occurs in combination with torsade de pointes or polymorphic ventricular tachycardia or signs/symptoms of serious arrhythmia, permanently discontinue ribociclib.

Interstitial Lung disease/Pneumonitis

Grade	Action
1 (asymptomatic)	No dose adjustment required. Initiate appropriate medical therapy and monitor
2 (symptomatic)	Withhold ribociclib until recovery to ≤Grade 1 then resume ribociclib at the next lower dose level if risk vs benefit is in favour of restarting treatment
3 or 4	Discontinue ribociclib

Any other toxicity

Grade	Action
1 or 2	No dose adjustment is required. Initiate appropriate medical therapy and monitor.
3	Withhold ribociclib until recovery to ≤Grade 1 then resume ribociclib at the same dose level. If Grade 3 toxicity recurs, resume ribociclib at next lower dose level
4	Discontinue ribociclib

Side Effects

Toxicity		MONALEESA-2		MONALEESA-3	
		Any grade (%)	G3 or 4 (%)	Any grade (%)	G3 or 4 (%)
Haematological	Neutropenia	74.3	59.3	69.6	53.4
	Anaemia	18.6	1.2	17.2	3.1
Non-haematological	Nausea	51.5	2.4	45.3	1.4
	Infections	50.3	4.2	NA	NA
	Fatigue	36.5	2.4	31.5	1.7
	Diarrhoea	35.0	1.2	29.0	0.6
	Alopecia	33.2	NA	18.6	0
	Vomiting	29.3	3.6	NA	NA
	Arthralgia	27.2	0.9	24.0	0.6
	Constipation	24.9	1.2	24.8	0.8
	Headache	22.2	0.3	21.5	0.8
	Hot flush	21.0	0.3	13.3	0
	Pruritis	NA	NA	19.9	0.2
	Back pain	19.8	2.1	17.6	1.7
	Cough	19.5	0	21.7	0.0
	Decreased appetite	18.6	1.5	16.1	0.2
	Rash	17.1	0.6	18.4	0.4
	Increased ALT	15.6	9.3	NA	NA
	Increased AST	15	5.7	NA	NA
	Pain in extremity	NA	NA	13.7	0.6
	Asthenia	NA	NA	NA	NA

Additional information

Nil

Significant drug interactions – for full details consult product literature/ reference texts

Strong CYP3A4 inhibitors (e.g. clarithromycin, intraconazole, ketoconazole, lopinavir, ritonavir, nefazodone, nelfinavir, posaconazole, telithromycin, verapamil, voriconazole): avoid concomitant treatment, use alternative concomitant medicine with less potential to inhibit CYP3A4. If concomitant use is unavoidable reduce ribociclib dose by 1 dose level (or omit for duration of strong CYP3A4 inhibitor therapy if on lowest dose level) and monitor closely for ribociclib toxicity. If strong CYP3A4 inhibitor is discontinued, increase ribociclib dose back to original dose after at least 5 half-lives of the CYP3A4 inhibitor.

Strong or moderate CYP3A4 inducers (e.g.phenytoin, rifampicin, carbamazepine, St John's Wort): decreased exposure of ribociclib risking loss of efficacy

CYP3A4 substrates (e.g. midazolam, ciclosporin, fentanyl, sirolimus, tacrolimus, simvastatin, amiodarone, quetiapine): increased plasma concentrations of substrate, avoid or refer to SmPC for CYP3A4 substrate for advice on dose modifications.

P-gp, BCRP, OATP1B1/1B3, OCT1, OCT2, MATE1 and BSEP transporter substrates e.g. digoxin, pravastatin, rosuvastatin, metformin: increased concentrations of substrate through transporter inhibition, monitor for increased toxicity from substrate.

Medicines that prolong QT interval e.g. amiodarone, sotalol, chloroquine, clarithromycin, ciprofloxacin, levofloxacin, azithromycin, methadone, ondansetron): avoid concomitant treatment due to risk of QT prolongation.

References

- National Institute for Health and Care Excellence TA496. Accessed 07 January 2026 via www.nice.org.uk
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- Summary of Product Characteristics Ribociclib (Novartis) accessed 07 January 2026 via www.medicines.org.uk
- Hortobagyi, G.N. *et al.* Overall Survival with Ribociclib plus Letrozole in Advanced Breast Cancer. N Engl J Med 2022; 386:942-950
- Slamon, D.J. *et al*. Overall Survival with Ribociclib plus Fulvestrant in Advanced Breast Cancer. N Engl J Med 2020; 382:514-524

Version	Issue date	Review date	Revision	Written/Checked/Authorised
2	Jan 2026	Jan 2029	Transferred to new template ECG guidance updated in line with SPC.	Written/reviewed: Kate Gregory (Lead Pharmacist for SACT protocols, SWAG Cancer Alliance) Checked: Dr J Braybrooke, (Consultant Oncologist, UHBW NHS Trust and SWAG Cancer Alliance) Authorised: Dr J Braybrooke, (Consultant Oncologist, UHBW NHS Trust and SWAG Cancer Alliance)

Schedule of investigations and treatment plan

Activity	Pre-tx	Cycle 1 D14	Cycle 2 D1	Cycle 2 D15	Cycle 3-6	Ongoing
Informed consent	X					
Clinical assessment	X		X		X	Every cycle
FBC	X	X	X	X	X	Every cycle
U&E & LFTs	X	X	X	X	X	Every cycle
CrCl	X	X	X	X	X	Every cycle
Calcium, Phosphate, Magnesium	X		X		X	As clinically indicated
Imaging as per guidance	X					Repeat if clinically indicated
ECG	X	X				If clinically indicated
Weight recorded	X					Repeat if necessary