Systemic Anti-Cancer Therapy Protocol

Acalabrutinib (monotherapy) Chronic Lymphocytic Leukaemia

PROTOCOL REF: MPHAAMCLLHA
(Version No: 1.1)

Approved for use in:

1. Acalabrutinib as monotherapy is recommended as an option for untreated chronic lymphocytic leukaemia (CLL) in adults, only if:
    - there is a 17p deletion or TP53 mutation, or
    - there is no 17p deletion or TP53 mutation, and fludarabine plus cyclophosphamide and rituximab (FCR), or bendamustine plus rituximab (BR) is unsuitable
2. Acalabrutinib as monotherapy is recommended, within its marketing authorization, as an option for previously treated CLL in adults.

Blueteq registration is required

Dosage:

Drug	Dose	Route	Frequency
Acalabrutinib capsule	**100mg**	Oral	Twice daily continuously

To continue until progression or unacceptable toxicity.

Administration:

- Can be taken with or without food
- Should be swallowed whole with a glass of water. Do not open, break, or chew capsules

- Should be taken either 2 hours before or 2 hours after any antacid medication or two hours before H2 receptor antagonists
- If more than 3 hours past usual dosing time, skip the missed dose and take the next dose of acalabrutinib at the regularly scheduled time. Do not take an extra dose to make up for a missed dose
- Consider withholding acalabrutinib for 3-7 days pre and post surgery depending on the type of surgery and the risk of bleeding

Anti-emetic risk:

Mildly emetogenic.

Supportive treatments:

Metoclopramide 10mg three times a day when required

Co-trimoxazole 480mg once daily

Allopurinol 300mg once daily for first month of therapy

Interactions:

Strong CYP3A Inhibitors (e.g. itraconazole and clarithromycin)	
Clinical Impact	• Co-administration of acalabrutinib with a strong CYP3A inhibitor increased acalabrutinib plasma concentration. • Increased acalabrutinib concentrations may result in increased toxicity.
Prevention or Management	• Avoid co-administration of strong CYP3A inhibitors with acalabrutinib. • Alternatively, if the inhibitor will be used short-term, interrupt acalabrutinib.
Moderate CYP3A Inhibitors (e.g. erythromycin, fluconazole, verapamil)	
Clinical Impact	• Co-administration of acalabrutinib with a moderate CYP3A inhibitor may increase acalabrutinib plasma concentrations. • Increased acalabrutinib concentrations may result in increased toxicity.
Prevention or Management	• When acalabrutinib is co-administered with moderate CYP3A inhibitors, reduce acalabrutinib dose to 100 mg once daily.
Strong CYP3A Inducers (e.g. phenytoin and rifampin)	
Clinical Impact	• Co-administration of acalabrutinib with a strong CYP3A inducer decreased acalabrutinib plasma concentrations.

	• Decreased acalabrutinib concentrations may reduce acalabrutinib activity.
Prevention or Management	• Avoid co-administration of strong CYP3A inducers with acalabrutinib. • If a strong CYP3A inducer cannot be avoided, increase the acalabrutinib dose to 200 mg approximately every 12hours.
Gastric Acid Reducing Agents	
Clinical Impact	• Co-administration of acalabrutinib with a proton pump inhibitor, H2- receptor antagonist, or antacid may decrease acalabrutinib plasma concentrations. • Decreased acalabrutinib concentrations may reduce acalabrutinib activity. • If treatment with a gastric acid reducing agent is required, consider using a H_2 receptor antagonist (e.g., ranitidine or famotidine) or an antacid (e.g., calcium carbonate).
Prevention or Management	Antacids: Separate dosing by at least 2 hours.
	H2-receptor antagonists: Take acalabrutinib 2 hours before taking the H2- receptor antagonist.
	Proton pump inhibitors: Avoid co-administration. Due to the long-lasting effect of proton pump inhibitors, separation of doses may not eliminate the interaction with acalabrutinib.

Main toxicities:

Thrombocytopenia, neutropenia, anaemia, nausea, vomiting, diarrhoea, serious infections, haemorrhage, secondary primary malignancies and atrial fibrillation.

Investigations and treatment plan

	Pre	Cycle 1	Cycle 2	Cycle 3+	Ongoing
Clinical Assessment	X	X	X	X	
SACT Assessment (including toxicity and performance status)		X	X	X	
FBC	X	X	X	X	Can reduce to 3 monthly with stable treatment
U&E & LFTs & Calcium profile	X	X	X	X	Can reduce to 3 monthly with stable treatment
CrCl (Cockcroft and Gault)	X				
Informed Consent	X				
ECG and ECHO	X				Patients with cardiac history or at risk of cardiac complications
CT scan	X				If clinically indicated
Bone marrow biopsy	X				If clinically indicated
Height	X				
Weight	X	X	X	X	
Pregnancy test	X				
Hepatitis B (including surface antigen and HB core antibody) and Hepatitis C testing	X				

Dose Modifications and Toxicity Management:

Haematological toxicity:

Adverse Reaction	Occurrence	Dose Modification
Platelets less than 50 x 10^9/L *and* bleeding OR platelets less than 25 x 10^9/L	First and Second	Interrupt acalabrutinib. Once toxicity has resolved to Grade 1 (platelets >75 x 10^9/L, ANC >1.5 x 10^9/L) or baseline level, acalabrutinib may be resumed at 100 mg approximately every 12 hours.
OR ANC less than 0.5 x 10^9/L lasting longer than 7 days (GCSF could be considered).	Third	Interrupt acalabrutinib. Once toxicity has resolved to Grade 1 (platelets >75 x 10^9/L, ANC >1.5 x 10^9/L) or baseline level, acalabrutinib may be resumed at a reduced frequency of 100 mg once daily.
	Fourth	Discontinue acalabrutinib.

These haematological guidelines assume that patients are well with good performance status, that other acute toxicities have resolved and the patient has not had a previous episode of neutropenic sepsis.

Dosing in renal and hepatic impairment:

Hepatic	
Severe	Avoid acalabrutinib
Renal	
CrCl < 30ml/min or dialysis	No data to support use

References:

Calquence (Acalabrutinib) Summary of Product Characteristics available at https://www.medicines.org.uk/emc Viewed 25th March 2021