SACT PROTOCOL

The Clatterbridge Cancer Centre NHS Foundation Trust

Systemic Anti Cancer Therapy Protocol

Imatinib
Gastro-Intestinal Stromal Tumours (GIST)

PROTOCOL REF: MPHAIGIST
(Version No. 1.0)

Approved for use in:

Palliative treatment for unresectable and/or metastatic malignant GIST as outlined in NICE TA86 and TA209.

Adjunctive treatment following surgery for up to 3 years in GIST with a high risk of recurrence as defined by the UK Clinical practice guideline and NICE TA326.

Dosage:

Drug	Dose	Route	Frequency
Imatinib tablets	**400mg**	PO	ONCE daily

Palliative treatment: until disease progression or untolerable toxicity

Adjunctive treatment: up to 3 years after surgery

Administration:

- Imatinib should be taken with food with a large glass of water to reduce the risk of gastrointestinal irritation
- Tablets can be dissolved in water or apple juice (200mL), stirred and drunk as soon as possible

- Imatinib should be discontinued 1 week before major surgery and restarted when risk of bleeding is considered to be minimal.

Emetogenic risk:

Low risk – prophylaxis not required

Supportive treatments:

N/A

Extravasation risk (if applicable):

Refer to the CCC policy for the 'Prevention and Management of Extravasation Injuries'

Dosing in renal and hepatic impairment:

Renal	Caution advised in renal impairment. Dose reduce when poorly tolerated.

Hepatic	Imatinib is primarily metabolised in the liver. Imatinib can be used with in mild / moderate / severe hepatic dysfunction. Dose reduce when poorly tolerated.

Interactions:

Imatinib is a substrate of CYP3A4. Inhibitors of CYP3A4 would be expected to increase plasma levels of imatinib so caution is advised if a combination is necessary. CYP3A4 inducers including dexamethasone, phenytoin, rifampicin, St John's Wort may significantly reduce exposure to imatinib. Strong CYP3A4 inducers should be avoided.

Imatinib inhibits CYP2D6, CYP2C9 and CYP3A4. Patients receiving medication with narrow therapeutic indexes which are substrates of CYP3A4 (e.g. ciclosporin, tacrolimus, sirolimus, fentanyl, alfentanil, bortezomib and docetaxel) or CYP2D6 (e.g. metoprolol) should be monitored and doses adjusted as appropriate.

Main toxicities:

Very Common: Thrombocytopenia, neutropenia, anaemia, Headache, periorbital oedema, dermatitis/eczema/rash

Common: Muscle cramps, febrile neutropenia, anorexia, Liver enzyme abnormalities insomnia severe fluid retention (pleural effusion, oedema, pulmonary oedema, ascites, superficial oedema), blurred vision, fatigue.

Investigations and treatment plan:

	Pre	Cycle 1	Cycle 2	Prior to cycle 3	Cycle 3	Ongoing
Informed Consent	X					Prior to treatment
Clinical Assessment	X				X	As clinically indicated
SACT Assessment (to include PS and toxicities)	X	X	X		X	Every cycle
On treatment review				X		
FBC	X	X	X		X	Every cycle
U&E & LFTs & Magnesium	X	X	X		X	Every Cycle
Height recorded	X					
Weight recorded	X	X	X		X	Every cycle
Hepatitis B (including surface antigen and HB core antibody) and Hepatitis C testing	X					Prior to treatment

Dose Modifications and Toxicity Management:

Haematological toxicity:

ANC ≤ 1.0 x 10^9/L Or PLT ≤ 75 x 10^9/L	1. Withold treatment until ANC ≥ 1.5 and PLT ≥ 75 x 10^9/L. 2. Resume Imatinib at previous dose. 3. In the event of recurrence of ANC ≤ 1.5 and/or platelets ≤ 75 repeat step 1 and resume Imatinib at reduced dose of 300 mg.

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.

Non- Haematological toxicity

Bilirubin > 3 x upper limit of normal (ULN) or Liver transaminases (AST/ALT) > 5 x ULN	Withold imatinib until Bil levels have returned to < 1.5 x ULN and AST/ALT< 2.5 x ULN. Resume treatment at a reduced dose of 300mg

References:

1. Novartis. Glivec 400mg film-coated tablets (Imatinib). Summary of Product Characteristics. Updated 19/05/2022. Accessed on 29/07/2022

2. Dosage Adjustment for Cytotoxics in Hepatic Impairment. January 2009 UCLH - Dosage Adjustment for Cytotoxics in Hepatic Impairment (Version 3 - updated January 2009)

3. Krens S D, Lassche, Jansman G F G A, et al. Dose recommendations for anticancer drugs in patients with renal or hepatic impairment. Lancet Oncol 2019; 20: e201–08.

4. NICE: TA84. Imatinib for the treatment of unresectable and/or metastatic gastro-intestinal stromal tumours. Published: 2004.

5. NICE: TA209. Imatinib for the treatment of unresectable and/or metastatic gastrointestinal stromal tumours. Published: 2010.

6. NICE: 326. Imatinib for the adjuvant treatment of gastrointestinal stromal tumours. Published: 2014.

7. Judson et al. UK clinical practice guidelines for the management of gastrointestinal stromal tumours (GIST). Clinical Sarcoma Research. 2017.

Circulation/Dissemination

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Version History

		Author name and designation	Summary of main changes
09/08/2022	**Version 1.0**	**Rob Challoner (Pharmacist)**	Author