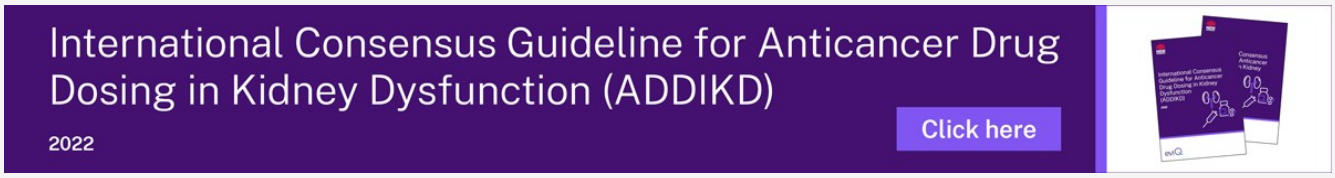
Primary myelofibrosis ruxolitinib

ID: 1509 v.3 **Endorsed**

This protocol is not exportable and does not have a calculator.

The anticancer drug(s) in this protocol may have been included in the ADDIKD guideline. Dose recommendations in kidney dysfunction have yet to be updated to align with the ADDIKD guideline. Recommendations will be updated once the individual protocol has been evaluated by the reference committee. For further information refer to the ADDIKD guideline. To assist with calculations, use the eviQ Estimated Glomerular Filtration Rate (eGFR) calculator.



Treatment schedule

Baseline Platelet Count (x 10^9/L)	Ruxolitinib starting dose	Route
50 to 100	5 mg TWICE a day with or without food	PO
100 to 200	15 mg TWICE a day with or without food	PO
Greater than 200	20 mg TWICE a day with or without food	PO

Continuous until disease progression or unacceptable toxicity

Starting dose recommendations: Link to Ho et al paper

- Determine the ruxolitinib starting dose based on platelet count, and titrate to a maximum dose of 25 mg TWICE a day based on response and tolerability with careful monitoring of platelet counts.
- In patients with initial platelet counts less than 50 x 10^9/L, when risk-benefit considerations warrant, ruxolitinib may be started at 5 mg daily, and platelets monitored closely.
- In patients with any hepatic impairment and/or moderate to severe renal impairment, the recommended starting dose based on platelet count should be reduced by 50%. The recommended starting dose for patients with polycythemia vera and severe renal impairment is 5 mg TWICE a day.

Notes:

- The dose is then titrated to a maximum dose of 25 mg TWICE a day based on response and tolerability with careful monitoring of platelet counts.
- Where possible, ruxolitinib should be given continuously without dose interruption, because of rapid symptom rebound on dose interruption. Gradual dose reduction is preferred over dose interruption, and determine dose based on the platelet count. (see table above).
- If efficacy is considered insufficient and blood counts are adequate, doses may be increased in 5 mg twice daily increments to a maximum dose of 25 mg twice daily. Doses should not be increased during the first 4 weeks of therapy and not more frequently than every 2 weeks. Discontinue treatment after 6 months if there is no spleen size reduction or symptom improvement since initiation of therapy with ruxolitinib.

Drug status: **Ruxolitinib:** (PBS authority)
Ruxolitinib is available as **5 mg, 10 mg, 15 mg** and **20 mg** tablets

Cost: ~ $4912 per month (based on 20 mg dose)

Indications and patient population

- High risk and intermediate-2 risk myelofibrosis (MF) (primary MF, post-polycythaemia vera MF or post-essential thrombocythemia MF)
- Intermediate-1 risk MF (primary MF, post-polycythaemia vera MF or post-essential thrombocythemia MF) with severe disease related symptoms that are resistant or refractory to other available therapies or when these cannot be tolerated

Clinical information

Caution with oral anti-cancer drugs	Select links for information on the safe prescribing, dispensing and administration of orally administered anti-cancer drugs. Read more about the COSA guidelines and oral anti-cancer therapy
Emetogenicity minimal or low	No routine prophylaxis required. If patients experience nausea and/or vomiting, consider using the low emetogenic risk regimen. Read more about preventing anti-cancer therapy induced nausea and vomiting
Progressive multifocal leukoencephalopathy	Progressive multifocal leukoencephalopathy (PML) have been reported with certain Tyrosine kinase inhibitors (e.g. ruxolitinib, ibrutinib). Patients should be closely monitored for new or worsening neuropsychiatric symptoms suggestive of PML. If PML is suspected treatment should be withheld pending appropriate investigation. Read more about progressive multifocal leukoencephalopthy and Therapeutic Goods Administration Medicines Safety update on progressive multifocal leukoencephalopathy from the Australian Government, Department of Health.
Infection risk	Inhibition of the JAK-STAT signalling may be associated with an increased risk of infection, and latent infections have been reported during treatment with ruxolitinib, such as hepatitis B, tuberculosis, latent mycobacterium avium complex (MAC) and varicella zoster. Pre-treatment screening and prophylaxsis is advised in at risk group patients.
Blood tests	FBC, EUC, eGFR, LFTs at baseline and repeat every 2 to 4 weeks until doses are stabilized, and then as clinically indicated.
Hepatitis B screening and prophylaxis	Routine screening for HBsAg and anti-HBc is recommended prior to initiation of treatment. Prophylaxis should be determined according to individual institutional policy. Read more about hepatitis B screening and prophylaxis in cancer patients requiring cytotoxic and/or immunosuppressive therapy
Vaccinations	Live vaccines are contraindicated in cancer patients receiving immunosuppressive therapy and/or who have poorly controlled malignant disease. Refer to the recommended schedule of vaccination for immunocompromised patients, as outlined in the Australian Immunisation Handbook. Read more about COVID-19 vaccines and cancer.
Fertility, pregnancy and lactation	Cancer treatment can have harmful effects on fertility and this should be discussed with all patients of reproductive potential prior to commencing treatment. There is a risk of foetal harm in pregnant women. A pregnancy test should be considered prior to initiating treatment in females of reproductive potential if sexually active. It is important that all patients of reproductive potential use effective contraception whilst on therapy and after treatment finishes. Effective contraception methods and adequate contraception timeframe should be discussed with all patients of reproductive potential. Possibility of infant risk should be discussed with breastfeeding patients. Read more about the effect of cancer treatment on fertility

Dose modifications

Evidence for dose modifications is limited, and the recommendations made on eviQ are intended as a guide only. They are generally conservative with an emphasis on safety. Any dose modification should be based on clinical judgement, and the individual patient's situation including but not limited to treatment intent (curative vs palliative), the anti-cancer regimen (single versus combination therapy versus chemotherapy versus immunotherapy), biology of the cancer (site, size, mutations, metastases), other treatment related side effects, additional co-morbidities, performance status and patient preferences.Suggested dose modifications are based on clinical trial findings, product information, published guidelines and reference committee consensus . The dose reduction applies to each individual dose and not to the total number of days or duration of treatment cycle unless stated otherwise. Non-haematological gradings are based on Common Terminology Criteria for Adverse Events (CTCAE) unless otherwise specified. Renal and hepatic dose modifications have been standardised where possible. For more information see dosing considerations & disclaimer .

Note:

- If efficacy is considered insufficient and blood counts are adequate, doses may be increased in 5 mg twice daily increments to a maximum dose of 25 mg twice daily, in patients with baseline platelet count ≥ 100 x 10^9/L and maximum dose of 10 mg twice daily in patients with baseline platelet count of 50 to < 100 x 10^9/L prior to initial treatment with ruxolitinib. Doses should not be increased during the first 4 weeks of therapy and not more frequently than every 2 weeks. Discontinue treatment after 6 months if there is no spleen size reduction or symptom improvement since initiation of therapy with ruxolitinib.
- All dose reductions are calculated as a percentage of the starting dose.

In patients with an initial platelet count of 50 to 100 x 10^9/L:[1]

- ruxolitinib should be commenced at 5 mg twice daily, incrementing by 5 mg every 4-weeks to a maximum of 10 mg twice daily
- dose increase should be limited to patients who maintain a platelet count of ≥ 35 x 10^9/L, have a platelet count reduction of less than 20% since last assessment and maintain ANC ≥ 1.0

Haematological toxicity[2]

If baseline platelet count ≥ 100 x 10^9/L prior to initial treatment with ruxolitinib

	Dose at time of platelet decline:				
	25 mg BD	**20 mg BD**	**15 mg BD**	**10 mg BD**	**5 mg BD**
Platelets x 10^9/L	**New dose:**				
100 to less than 125	20 mg BD	15 mg BD	No change	No change	No change
75 to less than 100	10 mg BD	10 mg BD	10 mg BD	No change	No change
50 to less than 75	5 mg BD	5 mg BD	5 mg BD	5 mg BD	No change
less than 50 *	Hold	Hold	Hold	Hold	Hold

** depending on patients individual bleeding risk, ruxolitinib may be continued at 5mg twice daily (or even 5mg daily) in patients with platelets count of < 50 x 10^9/L [1]*

- Treatment should be withheld if the platelet count falls below 50 x 10^9/L or the absolute neutrophil count (ANC) falls below 0.5 x 10^9/L.
- After recovery of blood counts above these levels, ruxolitinib may be restarted at 5 mg twice daily and gradually increased based on careful monitoring of blood cell counts.

If baseline platelet count 50 to < 100 x 10^9/L prior to initial treatment with ruxolitinib

Platelets x 10^9/L	
25 to less than 35 and platelet count decreased < 20% during prior 4 weeks	If current daily dose • > 5 mg: reduce dose by 5 mg once daily • 5 mg once daily: continue at 5 mg once daily
25 to less than 35 and platelet count decreased ≥ 20% during prior 4 weeks	If current daily dose: • > 10 mg: reduce dose by 5 mg twice daily • 5 mg twice daily: reduce dose to 5 mg once daily • 5 mg once daily: continue at 5 mg once daily
less than 25	Hold

Hepatic impairment

In patients with any hepatic impairment the recommended starting dose based on platelet count should be reduced by approximately 50%.

Hepatic impairment
Patients diagnosed with hepatic impairment while receiving ruxolitinib should be carefully monitored and may need to have their dose reduced to avoid adverse drug reactions. Ruxolitinib should be avoided in patients with hepatic impairment and platelet count less than 100 x 10^9/L.

Renal impairment	
Creatinine clearance (mL/min)	
less than 60	Consider reducing dose based on platelet count by 50%
less than 15 on dialysis	Limited data suggests, initial single dose of 15 mg or 20 mg (or two doses of 10 mg given 12 hours apart) based on platelet counts with subsequent single doses only after each dialysis session. Monitor closely for safety and efficacy.
less than 15 not undergoing dialysis *OR* moderate to severe renal impairment and platelet counts < 100 x 10^9/L	Avoid ruxolitinib

Interactions

Drug interactions in eviQ protocols are under review and being updated to align with current literature. Further site-wide updates and changes will occur in due course. References & Disclaimer

The drug interactions shown below are not an exhaustive list. For a more comprehensive list and for detailed information on specific drug interactions and clinical management, please refer to the specific drug product information and the following key resources:

- *MIMS - interactions tab (includes link to a CYP-450 table) (login required)*
- *Australian Medicines Handbook (AMH) – interactions tab (login required)*
- *Micromedex Drug Interactions (login required)*
- *Cancer Drug Interactions*
- *Cytochrome P450 Drug Interactions*

Ruxolitinib		
	Interaction	**Clinical management**
CYP3A4 inhibitors (e.g. aprepitant, azole antifungals, clarithromycin, erythromycin, grapefruit juice, ritonavir etc.)	Increased toxicity of ruxolitinib possible due to reduced clearance	Avoid combination or monitor for ruxolitinib toxicity and reduce the dose appropriately
CYP3A4 inducers (e.g. carbamazepine, phenytoin, phenobarbitone, rifampicin, St John's wort etc.)	Reduced efficacy of ruxolitinib possible due to increased clearance	Avoid combination or monitor for decreased clinical response to ruxolitinib
Drugs metabolised by CYP3A4 (e.g. atorvastatin, benzodiazepines, calcineurin inhibitors, clarithromycin, dihydroergotamine, simvastatin, etc.)	Increased effect/toxicity of these drugs possible due to inhibition of CYP3A4 by ruxolitinib resulting in reduced clearance	Avoid combination or monitor for increased effect/toxicity
Substances transported by P-glycoprotein or other transporters (e.g. cyclosporin, dabigatran, rosuvastatin, etc.)	Ruxolitinib may inhibit P-glycoprotein (P-gp) and breast cancer resistance protein (BCRP); plasma concentration of substrates of P-gp and/or BCRP may be increased when taken with ruxolitinib	Monitor for increased effect/toxicity

General		
	Interaction	**Clinical management**
Warfarin	Anti-cancer drugs may alter the anticoagulant effect of warfarin.	Monitor INR regularly and adjust warfarin dosage as appropriate; consider alternative anticoagulant.
Direct oral anticoagulants (DOACs) e.g. apixaban, rivaroxaban, dabigatran	Interaction with both CYP3A4 and P-gp inhibitors /inducers. DOAC and anti-cancer drug levels may both be altered, possibly leading to loss of efficacy or toxicity (i.e. increased bleeding).	Apixaban: avoid concurrent use with strong CYP3A4 and P-gp inhibitors. If treating VTE, avoid use with strong CYP3A4 and P-gp inducers. Rivaroxaban: avoid concurrent use with strong CYP3A4 and P-gp inhibitors. Dabigatran: avoid combination with strong P-gp inducers and inhibitors. If concurrent use is unavoidable, monitor closely for efficacy/toxicity of both drugs.
Digoxin	Anti-cancer drugs can damage the lining of the intestine; affecting the absorption of digoxin.	Monitor digoxin serum levels; adjust digoxin dosage as appropriate.
Antiepileptics	Both altered antiepileptic and anti-cancer drug levels may occur, possibly leading to loss of efficacy or toxicity.	Where concurrent use of an enzyme-inducing antiepileptic cannot be avoided, monitor antiepileptic serum levels for toxicity, as well as seizure frequency for efficacy; adjust dosage as appropriate. Also monitor closely for efficacy of the anti-cancer therapy.
Antiplatelet agents and NSAIDs	Increased risk of bleeding due to treatment related thrombocytopenia.	Avoid or minimise combination. If combination deemed essential, (e.g. low dose aspirin for ischaemic heart disease) monitor for signs of bleeding.
Serotonergic drugs, including selective serotonin reuptake inhibitors (SSRIs e.g. paroxetine) and serotonin noradrenaline reuptake inhibitors (SNRIs e.g. venlafaxine)	Increased risk of serotonin syndrome with concurrent use of 5-HT3 receptor antagonists (e.g. palonosetron, ondansetron, granisetron, tropisetron, dolasetron, etc.)	Avoid combination. If combination is clinically warranted, monitor for signs and symptoms of serotonin syndrome (e.g. confusion, agitation, tachycardia, hyperreflexia). For more information link to TGA Medicines Safety Update
Vaccines	Diminished response to vaccines and increased risk of infection with live vaccines.	Live vaccines (e.g. BCG, MMR, zoster and varicella) are contraindicated in patients on immunosuppressive therapy. Use with caution in patients on non-immunosuppressive therapy. For more information; refer to the recommended schedule of vaccination for cancer patients, as outlined in the Australian Immunisation Handbook

Administration

eviQ provides safe and effective instructions on how to administer cancer treatments. However, eviQ does not provide every treatment delivery option, and is unable to provide a comprehensive list of cancer treatment agents and their required IV line giving set/filter. There may be alternative methods of treatment administration, and alternative supportive treatments that are also appropriate. Please refer to the individual

product information monographs via the TGA website for further information.

Administration

This is an oral treatment

Safe handling and waste management (reproductive risk only)

Safe administration

General patient assessment prior to each treatment.

Any toxicity grade 2 or greater may require dose reduction, delay or omission of treatment and review by medical officer before recommencing treatment.

- baseline weight
- baseline urinalysis

Pre treatment medication

Verify antiemetics taken or administer as prescribed.

Treatment - Time out

Ruxolitinib

- administer orally TWICE a day
- swallow whole with a glass of water; do not break, crush or chew
- can be taken with or without food

Note: missed doses should not be replaced; if a tablet is forgotten or vomited, normal dosing should be resumed at the next scheduled dose.

Continue safe handling precautions (reproductive risk only) for 7 days after completion of drug(s).

Discharge information

Ruxolitinib tablets

- Ruxolitinib tablets with written instructions on how to take them.

Patient information

- Ensure patient receives patient information sheet.

Side effects

The side effects listed below are not a complete list of all possible side effects for this treatment. Side effects are categorised into the approximate onset of presentation and should only be used as a guide.

Immediate (onset hours to days)	
Headache	
Nausea and vomiting	Read more about prevention of treatment induced nausea and vomiting

Early (onset days to weeks)	
Abdominal pain	Dull ache, cramping or sharp pains are common with some anti-cancer drugs. These are caused by either increased or decreased gastrointestinal motility and can be associated with diarrhoea or constipation.
Dizziness	Feeling faint or lightheaded, weak or unsteady. Advise patients to stand up slowly from sitting down or lying down positions and increase fluid intake if dehydrated.
Hepatotoxicity	Anti-cancer drugs administered either alone or in combination with other drugs and/or radiation may cause direct or indirect hepatotoxicity. Hepatic dysfunction can alter the metabolism of some drugs resulting in systemic toxicity.
Hyperlipidaemia and hypercholesterolaemia	Abnormally elevated levels of lipids and cholesterol in the blood.
Hypertension associated with angiogenesis inhibitors	High blood pressure can occur with angiogenesis inhibitors and tyrosine kinase inhibitors.
Neutropenia	Abnormally low levels of neutrophils in the blood. This increases the risk of infection. Any fever or suspicion of infection should be investigated immediately and managed aggressively. Read more about immediate management of neutropenic fever
Thrombocytopenia	A reduction in the normal levels of functional platelets, increasing the risk of abnormal bleeding. Read more about thrombocytopenia

Late (onset weeks to months)	
Anaemia	Abnormally low levels of red blood cells (RBCs) or haemoglobin in the blood. Read more about anaemia
Progressive multifocal leukoencephalopathy (PML)	A rare opportunistic viral infection of the brain, usually leading to death or severe disability, can occur with monoclonal antibodies (e.g. rituximab, obinutuzumab, ofatumumab, brentuximab vedotin) and other targeted therapies (e.g. ibrutinib, ruxolitinib, idelalisib). Onset may occur up to months after the final dose. Read more about progressive multifocal leukoencephalopathy (PML)

Evidence

Myelofibrosis (MF) is myeloproliferative neoplasm that can present as a de novo disorder – primary myelofibrosis (PMF) or secondary to polycythaemia vera (PV) or essential thrombocythaemia (ET). Dysregulation of the Janus Associated kinases (JAK1 and JAK2) is observed. Approximately 90% of MF patients have one of the mutually exclusive driver mutations JAK2, CALR or MPL.[3] In addition, ASLX1, SRSF2, U2AF1Q57, EZH2 and IDH1/2 have been identified as high molecular risk (HMR) mutations and have been incorporated into the most recent international prognostic scoring system (MIPSS70+ V2.0).[4]

Ruxolitinib is a selective inhibitor of JAK1 and JAK2; its use is predominantly provided by the COMFORT-II and COMFORT-I studies. COMFORT-II was a multi-centre, randomised open-label, controlled phase III study that included adults with either PMF, post-PV-MF or post ET-MF, who had a palpable spleen of at least 5cm below the costal margin and no previous treatment with a JAK inhibitor.[5] Patients had a platelet count = $100x10^9$/L, peripheral blast count of <10%, ECOG 0-3 classed at intermediate-2 risk or high risk according to the IPSS with a life expectancy of 6 months.

Patients were not allogeneic transplant candidates. Cross-over was allowed.[5] Patients were randomized 2:1 to ruxolitinib or best available therapy (any commercially available agent or no therapy). The initial dose of ruxolitinib was based on a baseline platelet count = 200 x 10^9/L (15 mg BD) and >200 x 10^9/L (20 mg BD). The maximum dose was 25 mg BD if tolerated or reduced to manage toxicity (neutropenia or thrombocytopenia). Therapy was stopped if platelet count was <50 x 10^9/L. Patients remained on therapy until disease progression.

Primary endpoint was reduction of at least 35% in spleen volume from baseline at week 48, and the study demonstrated a spleen response of 28% (n=144) in the ruxolitinib group compared to 0% (n=72) in the best available therapy group, p<0.001.[6] At week 48, the mean change in spleen volume from baseline was a 30% decrease in the ruxolitinib group compared with a 7.3% increase in the best available therapy group. The median time to achieve a 35% reduction in spleen volume was 12.3 weeks in the ruxolitinib

group.[5]

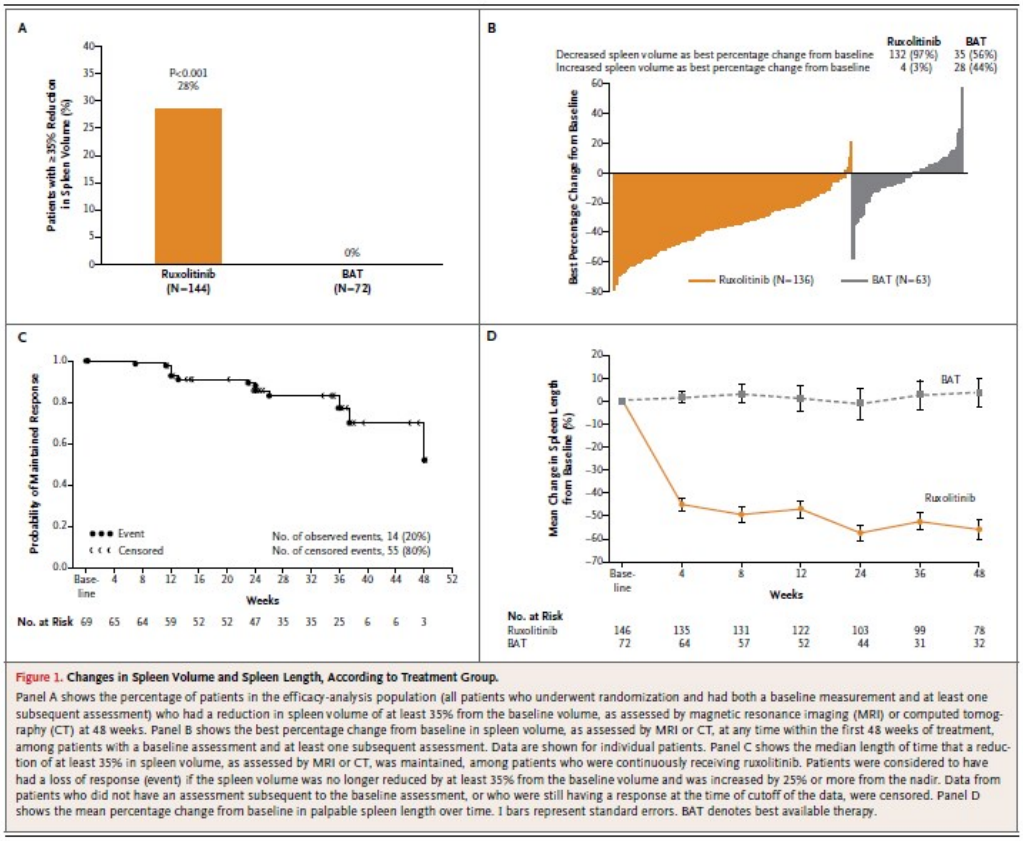


Figure 1. Changes in Spleen Volume and Spleen Length, According to Treatment Group.

Panel A shows the percentage of patients in the efficacy-analysis population (all patients who underwent randomization and had both a baseline measurement and at least one subsequent assessment) who had a reduction in spleen volume of at least 35% from the baseline volume, as assessed by magnetic resonance imaging (MRI) or computed tomography (CT) at 48 weeks. Panel B shows the best percentage change from baseline in spleen volume, as assessed by MRI or CT, at any time within the first 48 weeks of treatment, among patients with a baseline assessment and at least one subsequent assessment. Data are shown for individual patients. Panel C shows the median length of time that a reduction of at least 35% in spleen volume, as assessed by MRI or CT, was maintained, among patients who were continuously receiving ruxolitinib. Patients were considered to have had a loss of response (event) if the spleen volume was no longer reduced by at least 35% from the baseline volume and was increased by 25% or more from the nadir. Data from patients who did not have an assessment subsequent to the baseline assessment, or who were still having a response at the time of cutoff of the data, were censored. Panel D shows the mean percentage change from baseline in palpable spleen length over time. I bars represent standard errors. BAT denotes best available therapy.

Efficacy

At a median follow up of 151 weeks, Kaplan-Meier estimated probabilities of maintaining a spleen response at 48 and 144 weeks were 73% and 50% respectively.[7]At a median follow up of 3.5 years, analysis of the accrued 70 deaths (27% {40/146} ruxolitinib and 41% {30/73} best available therapy [BAT]) suggested a significant reduction in the risk of death for ruxolitinib, hazard ratio was 0.58 (95% CI: 0.36 to 0.93), p=0.022. Estimated survival probability at 3.5 years was 71% and 54% for ruxolitinib and best available therapy respectively.[8] The final 5-year analysis appears to show reduction in risk of death of ruxolitinib compared to BAT, but OS analysis was not feasible due to the cross-over design of the study.[9]

COMFORT-I was a double-blind, multi-centre, randomised, placebo-controlled, phase III study with similar inclusion and exclusion criteria as COMFORT-II, however, patients were not suitable for BAT and other treatments had been discontinued 4 weeks prior to the first baseline visit. Patients were randomised equally to ruxolitinib (n=155, dose regimen as per COMFORT-II) or matched placebo (n=154). The study remained blinded until the last randomized patient had undergone week 24 assessment and 50% of patients had a 36 week assessment, at which point placebo patients were eligible to crossover to ruxolitinib.

Primary outcome at week 24 for a 35% or more reduction in spleen volume was significantly greater in the ruxolitinib group (42%) compared with placebo group (0.7%), p<0.001.[10] After a median follow up of 149 weeks, the hazard ratio was 0.69 (95% CI: 0.46 to 1.03), p=0.067. In the final 5-year analysis, median OS was not reached in the ruxolitinib-randomised group (median follow up: 268.4 weeks), compared with 108 weeks in the placebo group (median follow-up: 269 weeks). These findings suggest that earlier treatment with ruxolitinib in patients with intermediate-II and high risk MF results in better outcomes.[11]

Overall, the final 5-year combined COMFORT I and II analysis supports ruxolitinib as an effective long-term treatment option for patients with intermediate-2 or high-risk myelofibrosis.[11]

Finally, ROBUST, a UK, open-label, phase II study, evaluated the safety and efficacy of ruxolitinib of 48 patients myelofibrosis (intermediate-I, II and high-risk). Consistent with results from COMFORT studies, ROBUST demonstrated treatment success (including spleen size reduction and symptom improvement) in 50% of patients (57% in Intermediate-I).[12]

Finally, ruxolitinib may be beneficial in terms of splenomegaly, symptoms and survival in patients with HMR mutations, although evidence is currently conflicting and further studies are warranted.[13, 14]

Toxicity

During the randomized phase of COMFORT-II, haematological adverse events such as anaemia and thrombocytopenia occurred

more frequently in the ruxolitinib patients and were managed by dose modification and/or red cell transfusion rather than treatment discontinuation. After 3 years follow-up, the rate of haematological adverse events (ie anaemia and thrombocytopenia) and other adverse events of special interest (bleeding and infection) were greatest in the first 6 months of therapy and reduced over time.[7] At 5 years follow-up, adverse events leading to study drug discontinuation were reported in 25% of patients. Combined 5-year follow-up COMFORT I and II analysis did not demonstrate any new or unexpected adverse events.[9, 11]

Herpes Zoster infections occurred at higher rates among patients treated with ruxolitinib compared with placebo, increasing with duration of exposure (0-12 months: 2.1%, >48 months: 10.3%). However, all were Grade ≤2 and clinical significance is unclear.[9]

Leukaemic transformation occurred in 3.4% of ruxolitinib and 5.5% of best available therapy patients.[7] At 5 years, leukaemic transformation occurred in 1.9% of ruxolitinib patients, with a decreased risk as compared to best available therapy in COMFORT-II, although the difference in exposure times and subsequent treatments in the best available therapy group made interpretation difficult.[9]

More recently, ruxolitinib has been shown to be efficacious and safe in patients baseline platelet counts 50-100 and < 50 during therapy without drug interruption. Some of these patients had a definite increase above the baseline platelet count after initial decline, suggesting that the thrombocytopenia is due to other factors than rather than just insufficient platelet production due to marrow fibrosis.[15, 1, 16]

References

1 Talpaz, M., R. Paquette, L. Afrin, et al. 2013. "Interim analysis of safety and efficacy of ruxolitinib in patients with myelofibrosis and low platelet counts." J Hematol Oncol 6(1):81.

2 Ruxolitinib: Drug information, Lexicomp, viewed 13 December 2018, https://www.uptodate.com.acs.hcn.com.au/contents/ruxolitinib-drug-information?search=ruxolitinib&source=panel_search_result&selectedTitle=1~27&usage_type=panel&kp_tab=drug_general&display_rank=

3 Tefferi, A., M. Nicolosi, M. Mudireddy, et al. 2018. "Driver mutations and prognosis in primary myelofibrosis: Mayo-Careggi MPN alliance study of 1,095 patients." Am J Hematol 93(3):348-355.

4 Tefferi, A. and A. Pardanani. 2011. "Serious adverse events during ruxolitinib treatment discontinuation in patients with myelofibrosis." Mayo Clin Proc 86(12):1188-1191.

5 Harrison, C., J. J. Kiladjian, H. K. Al-Ali, et al. 2012. "JAK inhibition with ruxolitinib versus best available therapy for myelofibrosis." N Engl J Med 366(9):787-798.

6 Ho, P. J., P. Marlton, C. Tam, et al. 2015. "Practical management of myelofibrosis with ruxolitinib." Intern Med J 45(12):1221-1230.

7 Cervantes, F., A. M. Vannucchi, J. J. Kiladjian, et al. 2013. "Three-year efficacy, safety, and survival findings from COMFORT-II, a phase 3 study comparing ruxolitinib with best available therapy for myelofibrosis." Blood 122(25):4047-4053.

8 Geyer, H. L. and R. A. Mesa. 2014. "Therapy for myeloproliferative neoplasms: when, which agent, and how?" Blood 124(24):3529-3537.

9 Harrison, C. N., A. M. Vannucchi, J. J. Kiladjian, et al. 2016. "Long-term findings from COMFORT-II, a phase 3 study of ruxolitinib vs best available therapy for myelofibrosis." Leukemia 30(8):1701-1707.

10 Verstovsek, S., R. A. Mesa, J. Gotlib, et al. 2012. "A double-blind, placebo-controlled trial of ruxolitinib for myelofibrosis." N Engl J Med 366(9):799-807.

11 Verstovsek, S., R. A. Mesa, J. Gotlib, et al. 2017. "Long-term treatment with ruxolitinib for patients with myelofibrosis: 5-year update from the randomized, double-blind, placebo-controlled, phase 3 COMFORT-I trial." J Hematol Oncol 10(1):55.

12 Mead, A. J., D. Milojkovic, S. Knapper, et al. 2015. "Response to ruxolitinib in patients with intermediate-1-, intermediate-2-, and high-risk myelofibrosis: results of the UK ROBUST Trial." Br J Haematol 170(1):29-39.

13 Guglielmelli, P., F. Biamonte, G. Rotunno, et al. 2014. "Impact of mutational status on outcomes in myelofibrosis patients treated with ruxolitinib in the COMFORT-II study." Blood 123(14):2157-2160.

14 Patel, K. P., K. J. Newberry, R. Luthra, et al. 2015. "Correlation of mutation profile and response in patients with myelofibrosis treated with ruxolitinib." Blood 126(6):790-797.

15 Bjorn, M. E., M. O. Holmstrom and H. C. Hasselbalch. 2016. "Ruxolitinib is manageable in patients with myelofibrosis and severe thrombocytopenia: a report on 12 Danish patients." Leuk Lymphoma 57(1):125-128.

16 Grunwald, M. R. and J. L. Spivak. 2016. "Ruxolitinib Enhances Platelet Production in Patients With Thrombocytopenic Myelofibrosis." J Clin Oncol 34(5):e38-40.

History

Version 3

Date	Summary of changes
20/05/2016	New protocol taken to Haematology Reference Committee meeting.
20/10/2016	Approved and published on eviQ.
31/05/2017	Transferred to new eviQ website. Version number change to v.2.
21/09/2018	Protocol reviewed at Haematology Reference Committee meeting.
05/06/2019	Evidence and dose modification sections updated. Version number changed to v.3. Review in 2 years.
23/10/2020	Protocol reviewed electronically by the Haematology Reference Committee, no changes. Review in 4 years.
21/12/2021	Changed antiemetic clinical information block to minimal or low, to align with new categories. See ID 7 Prevention of anti-cancer therapy induced nausea and vomiting (AINV) v5.

First approved: 20 October 2016
Last reviewed: 23 October 2020
Review due: 31 December 2024

The currency of this information is guaranteed only up until the date of printing, for any updates please check:
https://www.eviq.org.au/p/1509
31 Aug 2023

Patient information - Primary myelofibrosis - Ruxolitinib

Patient's name:

Your treatment

The treatment schedule below explains how the drug for this treatment is given.

Ruxolitinib		
This treatment is continuous. Your doctor will advise you how long to take the treatment for.		
Day	**Treatment**	**How it is given**
Continuous	**Ruxolitinib** *(rux-oh-LI-ti-nib)*	Take orally TWICE a day, at the same time each day, with or without food. Swallow whole with a large glass of water, do not break, crush or chew. If you forget to take a tablet or vomit a tablet, take your normal dose the next time it is due. Do not take an extra dose.

When to get help

Anticancer drugs (drugs used to treat cancer) can sometimes cause serious problems. It is important to get medical help immediately if you become unwell.

IMMEDIATELY go to your nearest hospital Emergency Department, or contact your doctor or nurse if you have any of the following at any time:	**Emergency contact details** Ask your doctor or nurse from your treating team who to contact if you have a problem
• a temperature of 38°C or higher • chills, sweats, shivers or shakes • shortness of breath • uncontrolled vomiting or diarrhoea • pain, tingling or discomfort in your chest or arms • you become unwell.	Daytime:..... Night/weekend:..... Other instructions:..... ....

Other information about your treatment

Changes to your dose or treatment delays

Sometimes a treatment may be started at a lower dose or the dose needs to be changed during treatment. There may also be times when your treatment is delayed. This can happen if your doctor thinks you are likely to have severe side effects, if you get severe side effects, if your blood counts are affected and causing delays in treatment, or if you are finding it hard to cope with the treatment. This is called a dose reduction, dose change or treatment delay. Your doctor will explain if you need any changes or delays to your treatment and the reason why.

Blood tests and monitoring

You will need to have a blood test before you start treatment and regularly throughout your treatment. Your doctor or nurse will tell you when to have these blood tests.

Other medications given during this treatment

- **Anti-sickness (anti-nausea) medication:** you may be given some anti-sickness medication. Make sure you take this medication as your doctor or nurse tells you, even if you don't feel sick. This can help to prevent the sickness starting.
- **Prophylaxis medication:** you may need to take some medications to prevent infection and to help prevent or reduce some of the side effects of the chemotherapy. Your doctor or nurse will tell you how and when to take these medications.

Side effects

Cancer treatments can cause damage to normal cells in your body, which can cause side effects. Everyone gets different side effects, and some people will have more problems than others.

The table below shows some of the side effects you may get with this treatment. You are unlikely to get all of those listed and you may also get some side effects that have not been listed.

Tell your doctor or nurse about any side effects that worry you. Follow the instructions below and those given to you by your doctor or nurse.

Immediate (onset hours to days)	
Headache	• You can take paracetamol if you have a headache. • **Tell your doctor or nurse immediately, or go to the nearest hospital Emergency Department if you get a very bad headache that is not helped by pain medication.**
Nausea and vomiting	• You may feel sick (nausea) or be sick (vomit). • Take your anti-sickness medication as directed even if you don't feel sick. • Drink plenty of fluids (unless you are fluid restricted). • Eat small meals more frequently. • Try food that does not require much preparation. • Try bland foods like dry biscuits or toast. • Gentle exercise may help with nausea. • Ask your doctor or nurse for eviQ patient information - Nausea and vomiting during cancer treatment. • **Tell your doctor or nurse immediately, or go to the nearest hospital Emergency Department if you have uncontrolled vomiting or feel dizzy or light-headed.**

Early (onset days to weeks)	
Stomach pain	• You may get: ◦ dull aches ◦ cramping or pain ◦ bloating or flatulence (gas). • **Tell your doctor or nurse immediately, or go to the nearest hospital Emergency Department if you have stomach pain that you are unable to control.**
Dizziness or feeling light-headed	• You may feel dizzy or light-headed. • These symptoms may be caused by your treatment, or other problems like dehydration. • If you are feeling dehydrated, drink plenty of fluids (unless you are fluid restricted) as this can be a cause of dizziness. • If you are feeling dizzy, try lying down until the dizziness passes. • When you want to get up from a sitting or lying down position, get up slowly to let your body adjust to the new position. • Tell your doctor or nurse if you get any of the symptoms listed above.

Liver problems	• You may get:
	  ◦ yellowing of your skin or eyes
	  ◦ itchy skin
	  ◦ pain or tenderness in your stomach
	  ◦ nausea and vomiting
	  ◦ loss of appetite
	• You will have regular blood tests to check how well your liver is working.
	• **Tell your doctor or nurse as soon as possible if you notice that your urine is a dark colour, the whites of your eyes look yellow, or if you have stomach pain.**

High blood cholesterol levels	• This treatment may increase your blood cholesterol levels. This is not a side effect you will notice. • Your cholesterol levels will be checked during your treatment.
High blood pressure (hypertension)	• You may not have any signs or symptoms if you have high blood pressure. • If it is severe you may get headaches, shortness of breath or feel dizzy. • Your blood pressure will be taken regularly during your treatment. • **Tell your doctor or nurse immediately, or go to the nearest hospital Emergency Department if you get any of the signs or symptoms listed above.**

Infection risk (neutropenia)	• This treatment lowers the amount of white blood cells in your body. The type of white blood cells that help to fight infection are called neutrophils. Having low level of neutrophils is called neutropenia. If you have neutropenia, you are at greater risk of getting an infection. It also means that your body can't fight infections as well as usual. This is a serious side effect, and can be life threatening.
	• Wash your hands often.
	• Keep a thermometer at home and take your temperature regularly, and if you feel unwell.
	• Do your mouth care regularly.
	• Inspect your central line site (if you have one) daily for any redness, pus or swelling.
	• Limit contact with people who are sick.
	• Learn how to recognise the signs of infection.
	• Ask your doctor or nurse for eviQ patient information - Infection during cancer treatment.
	• **Tell your doctor or nurse immediately, or go to the nearest hospital Emergency Department if you get any of the following signs or symptoms:**
	  ◦ **a temperature of 38°C or higher**
	  ◦ **chills, shivers, sweats or shakes**
	  ◦ **a sore throat or cough**
	  ◦ **uncontrolled diarrhoea**
	  ◦ **shortness of breath**
	  ◦ **a fast heartbeat**
	  ◦ **become unwell even without a temperature.**

Low platelets (thrombocytopenia)	• This treatment lowers the amount of platelets in your blood. Platelets help your blood to clot. When they are low, you are at an increased risk of bleeding and bruising. • Try not to bruise or cut yourself. • Avoid contact sport or vigorous exercise. • Clear your nose by blowing gently. • Avoid constipation. • Brush your teeth with a soft toothbrush. • Don't take aspirin, ibuprofen or other similar anti-inflammatory medications unless your doctor tells you to. • Tell your doctor or nurse if you have any bruising or bleeding. • **Tell your doctor or nurse immediately, or go to your nearest hospital Emergency Department if you have any uncontrolled bleeding.**

Late (onset weeks to months)	
Low red blood cells (anaemia)	• You may feel dizzy, light-headed, tired and appear more pale than usual. • Tell your doctor or nurse if you have any of these signs or symptoms. You might need a blood transfusion. • **Tell your doctor or nurse immediately, or go to the nearest hospital Emergency Department if you have any chest pain, trouble breathing, or feel like your heart is racing.**
Changes in the way your brain works [progressive multifocal leukoencephalopathy (PML)]	• This treatment can affect your central nervous system. This can be very serious. • **Tell your doctor or nurse immediately, or go to the nearest hospital Emergency Department if you get any of the following symptoms:** ◦ **trouble with your speech or vision** ◦ **confusion or memory loss** ◦ **changes in your personality** ◦ **weakness in your arms and legs** ◦ **poor balance or coordination** ◦ **fits (seizures).**

General advice for people having cancer treatment

Chemotherapy safety

- Learn how to keep you and your family safe while you are having anticancer drugs.
- See our patient information sheet - Chemotherapy safety at home.

Blood clot risk

- Cancer and anticancer drugs can increase the risk of a blood clot (thrombosis).
- Tell your doctor if you have a family history of blood clots.
- A blood clot can cause pain, redness, swelling in your arms or legs, shortness of breath or chest pain.
- If you have any of these symptoms go to your nearest hospital Emergency Department.

Medications and vaccinations

- Before you start treatment, tell your doctor about any medications you are taking, including vitamins or herbal supplements.
- Don't stop or start any medications during treatment without talking to your doctor and pharmacist first.
- Paracetamol is safe to take if you have a headache or other mild aches and pains. It is recommended that you avoid taking aspirin, ibuprofen and other anti-inflammatory type medications for pain while you are having treatment. However, if these medications have been prescribed by your doctor, do not stop taking them without speaking with your doctor.
- Vaccinations such as flu and tetanus vaccines are safe to receive while having treatment. Do not have any live vaccines during your treatment or for 6 months after it finishes. If you are unsure, check with your doctor before you have any vaccinations.
- People you live with should be fully vaccinated, including having live vaccines according to the current vaccination schedule. Extra care needs to be taken with hand washing and careful disposal of soiled nappies for infants who have recently received the rotavirus vaccine.

Other medical and dental treatment

- If you go to hospital or any other medical appointment (including dental appointments), always tell the person treating you that you are receiving anticancer drugs.
- Before you have any dental treatment, talk to your doctor.

Diet and food safety

- While you are receiving this treatment, it is important that you try to maintain a healthy diet.
- Grapefruit and grapefruit juice can interact with your medication and should be avoided while you are on this treatment.
- Speak to your doctor or nurse about whether drinking alcohol is safe with your treatment.
- If you have any concerns about recent weight loss or weight gain or questions about your diet, ask to speak to a dietitian.
- There are some foods that may cause infection in high risk individuals and should be avoided. For further information on foods to avoid and food hygiene please ask for a copy of the Listeria and food brochure.

Fertility

- Some cancer treatments can reduce your fertility. This can make it difficult or impossible to get pregnant or father a child.
- Talk to your doctor or nurse before you start any treatment. Depending on your situation there may be fertility sparing options available to you and/or your partner, discuss these with your doctor or nurse.

Pregnancy and breastfeeding

- Some cancer treatments can be dangerous to unborn babies. Talk to your doctor or nurse if you think there is any chance that you could be pregnant.
- Do not try to get pregnant or father a child during this treatment. Contraception should be used during treatment and after stopping treatment. Ask your doctor or nurse about what type of contraception you should use.
- If you are planning pregnancy/fatherhood after completing this treatment, talk to your doctor. Some doctors advise waiting between 6 months and 2 years after treatment.
- Do not breastfeed if you are on this treatment, as anti-cancer medications can also pass into breast milk.

Sex life and sexuality

- The desire to have sex may decrease as a result of this treatment or its side effects.
- Your emotions and the way you feel about yourself may also be affected by this treatment.
- It may help to discuss your concerns with your partner and doctor or nurse.

Quitting smoking

- It is never too late to quit smoking. Quitting smoking is one of the best things you can do to help your treatment work better.
- There are many effective tools to improve your chances of quitting.
- Talk to your treating team for more information and referral to a smoking cessation support service.

Staying active

- Research shows that exercise, no matter how small, has many benefits for people during and after cancer treatment.
- Talk to your doctor before starting an exercise program. Your doctor can advise whether you need a modified exercise program.

For more information about cancer treatment, side effects and side effect management see our Patient and carers section.

Where to get more information

Telephone support

- Call Cancer Council on 13 11 20 for cancer information and support
- Call the Leukaemia Foundation on 1800 620 420 (Mon to Fri 9am – 5pm)
- Call the Lymphoma Nurse Support Line on 1800 953 081 (Mon to Fri 9am - 5pm)
- Call the Myeloma Australia Support Line on 1800 693 566 (Mon to Fri 9am - 5pm)

Haematology, transplant and cellular therapy information

- Arrow bone marrow transplant foundation – arrow.org.au
- Australasian Menopause Society – menopause.org.au
- Chris O'Brien Lifehouse - Total Body Irradiation - mylifehouse.org.au/departments/radiation-oncology/total-body-irradiation/
- Healthy Male Andrology Australia – healthymale.org.au/
- International Myeloma Foundation – myeloma.org
- Leukaemia Foundation – leukaemia.org.au
- Lymphoma Australia – lymphoma.org.au
- Myeloma Australia – myeloma.org.au
- NSW Agency for Clinical Innovation, Blood & Marrow Transplant Network – https://aci.health.nsw.gov.au/networks/bmtct
- NSW Agency for Clinical Innovation - aci.health.nsw.gov.au/projects/immune-effector-cell-service
- NCCN Guidelines for Patients Immunotherapy Side Effects: CAR T-Cell Therapy - nccn.org/patientresources/patient-resources/guidelines-for-patients
- Talk Blood Cancer – cmlsupport.org.uk/organisation-type/social-media-groups

General cancer information and support

- Australian Rare Cancer (ARC) Portal – arcportal.org.au/
- Beyondblue – beyondblue.org.au

- Cancer Australia – canceraustralia.gov.au
- Cancer Council Australia – cancer.org.au
- Cancer Voices Australia – cancervoicesaustralia.org
- CanTeen – canteen.org.au
- Carers Australia – carersaustralia.com.au
- Carer Help - carerhelp.com.au
- eviQ Cancer Treatments Online – eviQ.org.au
- Food Standards Australia New Zealand: Listeria & Food Safety – foodstandards.gov.au/publications/pages/listeriabrochuretext.aspx
- LGBTQI+ People and Cancer - cancercouncil.com.au/cancer-information/lgbtqi
- Look Good Feel Better – lgfb.org.au
- Patient Information - patients.cancer.nsw.gov.au
- Radiation Oncology Targeting Cancer - targetingcancer.com.au
- Redkite – redkite.org.au
- Return Unwanted Medicines – returnmed.com.au
- Staying active during cancer treatment – patients.cancer.nsw.gov.au/coping-with-cancer/physical-wellbeing/staying-active

Quit smoking information and support

Quitting smoking is helpful even after you have been diagnosed with cancer. The following resources provide useful information and support to help you quit smoking. Talk to your treating team about any other questions you may have.

- Call Quitline on 13 QUIT (13 78 48)
- iCanQuit – iCanQuit.com.au
- Patient Information - patients.cancer.nsw.gov.au/coping-with-cancer/physical-wellbeing/quitting-smoking
- Quitnow – quitnow.gov.au

Additional notes:

First approved: 20 October 2016
Last reviewed: 23 October 2020
Review due: 31 December 2024

The currency of this information is guaranteed only up until the date of printing, for any updates please check:
https://www.eviq.org.au/pi/1509
31 Aug 2023