

Supplementary Materials

ITC results for efficacy outcomes used in costing

Bleeding and rescue medication use were based on the ITC matching the ROMI trial to the EPAG trial

(Table S1. ITC results for outcomes used in costing)

Sub-group		Value in the model				
		EPAG	ROMI	W&R	OR (95% CI): EPAG/W&R	OR (95% CI): ROMI/W&R
All patients	<i>Number of patients</i>	135	84	62+41		
	<i>Severe bleeding (WHO 3-5)</i>	2.2%	3.7%	6.5%	0.33 (0.07, 1.52)	0.55 (0.16, 1.93)
	<i>All bleeding (WHO 2-5)</i>	8.9%	5.7%	14.5%	0.57 (0.23, 1.45)	0.35 (0.15, 0.85)
	<i>Moderate bleeding only (WHO 2)</i>	6.7%	2.8%	8.1%	0.81 (0.26, 2.54)	0.32 (0.11, 0.94)
Splenuctomized	<i>Number of patients</i>	50	42	21+21		
	<i>Severe bleeding (WHO 3-5)</i>	1.0%	4.5%	9.5%	0.10 (0.00, 2.23)	0.45 (0.10, 2.00)
	<i>All bleeding (WHO 2-5)</i>	8.0%	9.4%	19.0%	0.37 (0.08, 1.65)	0.44 (0.14, 1.40)
	<i>Moderate bleeding only (WHO 2)</i>	7.0%	5.7%	9.5%	0.72 (0.12, 4.40)	0.57 (0.14, 2.41)
Non-Splenuctomized	<i>Number of patients</i>	85	42	41+20		
	<i>Severe bleeding (WHO 3-5)</i>	3.5%	4.6%	4.9%	0.71 (0.11, 4.44)	0.95 (0.08, 11.14)
	<i>All bleeding (WHO 2-5)</i>	9.4%	3.3%	12.2%	0.75 (0.23, 2.45)	0.25 (0.06, 1.00)
	<i>Moderate bleeding only (WHO 2)</i>	5.9%	1.2%	7.3%	0.79 (0.18, 3.49)	0.15 (0.03, 0.86)
All patients	<i>Use of rescue medication</i>	18.0%	10.4%	40.0%	0.33 (0.17, 0.64)	0.17 (0.08, 0.39)

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Primary costs

Table S2. Primary therapy dosing schedule

Drug	Kg or M2	Form	Dosing information	Indicated dose (mg for oral, mg/2 for IV)	Mean dose in trial	Dose intensity	Final dose	Dosing schedule per week	Treatment duration in weeks
Eltrombopag		Oral	mg	50	55	100.0%	55	7	26
Romiplostim	81	IV	ug/kg	2	317	100.0%	317	1	26
Rituximab**	1.7	IV	mg/m2	375	638	100.0%	638	1	4

**Assuming 4 weeks of therapy

Table S3. Primary therapy costs

Drug	Cost per Pack	Unit per pack	Unit strength	Price per unit	Pack needed	Administration costs per week*	Cost per week	Total Administration cost	Total cost (all treatment duration)
Eltrombopag†	10,253.00	30	75	342	6.07	0.00	2,392	0	62,202
Romiplostim†	6,492.00	4	250	1623	13.0	75.2	3,321	1,955	84,396
Rituximab†	1,720.59	10	20	172	12.8	222.3	5,728	889	22,024

†Source: Novartis internal pricing database

Administration costs

Subcutaneous injection and IV administration costs were obtained from the CMS Medicare Fee Schedule. Romiplostim administration was based on subcutaneous injection costs. IV administration (used for rituximab) were assumed to be delivered within one hour. It was assumed that orally-delivered therapies had no administrative cost.

Table S4. Administration costs

Drug	Cost per Pack
Oral cost	0.00
Subcutaneous	75.19
IV first hour	136.41
IV additional hours	28.64

Routine care costs

Laboratory visits, office visits, outpatient visits, and emergency department visits were included in the model.

To calculate the cost of each service, Saleh *et al* cost estimates were inflation-adjusted based on an inflation rate of 3.6% over 7 years, and were adjusted to reflect costs for a 26-week period (since their estimates were based on a year-long time horizon).

Table S5. Routine care costs

Resource	Mean resource use (yearly)	% Related to ITP	Unit cost	Final adjusted value	Final unit costs	Final cost for 26 weeks and inflated
Laboratory visits	0.9	10.70%	Platelet: \$6.11	0.048	27.00	17.91

Hepatic: \$11.13						
Office visits	2.1	18.20%	\$50.84 (Assumed in facility)	0.191	78.00	51.75
Other outpatient visits	1.1	28.20%	\$75.19 (Non-facility)	0.155	367.00	243.51
Emergency department visits	0.5	52%	\$62.66	0.130	260.00	172.51
						485.69

Source: Saleh et al (2009)

Rescue treatment costs

Wastage was included for the rescue treatment estimates (ie it was assumed that no vial sharing or “pill-splitting” took place).

Table S6. Rescue medication dosing and costs

Dosing schedule								
Drug	Kg or M2	Form	Dosing information	Dosing (mg for oral, mg/2 for IV)	Indicated dose	Dose intensity	Final total dose	Dosing schedule
IVIg	81	IV	1 g/kg for 2 days	81	81	100.0%	162	2
IV methylprednisolone	81	IV	4 X 40 mg	40	40	100.0%	160	4

Drug costs									
Drug	Cost per Pack	Unit per pack	Unit strength	Price per unit	Pack needed (Wastage included)	Administration costs total	Utilization*	Total cost (all treatment durations)	Source
Blood Transfusion				424.9			24.4%	104	Utilization: Lee et al (2013) Cost: Toner et al (2011)
Rescue medications									
IVIg	37.89	1	0.5	38	324.00	272.82	40.0%	12,549	Utilization: Cheng et al (2013)

										Cost: Medicare ASP Drug Pricing Files
IV methylprednisolone	3.73	1	40	4	4.00	545.6	60.0%	561	Utilization: Cheng et al (2013)	Cost: Medicare ASP Drug Pricing Files
Total									5,460	
<i>Source of utilization: Lee et al (2013)</i>										
<i>*Per Cheng et al (2011), 60% received corticosteroids</i>										

Table S7. Summary rescue medication costs

Drug	% with Rescue Medication	Average Costs
Eltrombopag	18.0%	982.77
Romiplostim	10.4%	568.99
Watch and rescue	40.0%	2,183.93

Bleeding related costs

Costs per bleeding event (with and without hospitalization) were based on Lin et al (2017) estimates.

Table S8. Bleeding related costs (all patients)

Drug	Severe/significant bleeding	Moderate bleeding events	Average costs of G3-5 bleedings	Average costs of G2 bleedings	All bleeding costs
Eltrombopag	2.2%	6.7%	990.89	146.40	1,137.29
Romiplostim	3.7%	2.8%	1,640.48	60.55	1,701.02
Watch and rescue	6.5%	8.1%	2,876.78	177.09	3,053.87

Adverse event costs

Adverse event (AE) prevalence was based on the respective clinical trials for each comparator.

Only all grade AEs reported in $\geq 20\%$ of patients were included in the model, as serious AE data were not available for all comparators.

Table S9. Adverse event prevalence and costs

Adverse Events	Eltrombopag	Romiplostim	Watch and Rescue	Unit Costs
Arthralgia	7.0%	26.0%	5.0%	14,109.26
Confusion	1.0%	25.0%	5.0%	26,260.18
Diarrhea	13.0%	17.0%	10.0%	8,032.65
Epistaxis	5.0%	32.0%	10.0%	32,356.37
Fatigue	10.0%	33.0%	13.0%	6,297.79
Headache	30.0%	35.0%	33.0%	27,715.11
Infusion Reactions	0.0%	0.0%	0.0%	8,615.54
Pain in Extremities	7.0%	13.0%	10.0%	14,109.26
Petechiae	0.0%	17.0%	0.0%	14,109.26
Upper respiratory tract infection	10.0%	17.0%	11.0%	21,094.77

Cost source: HCUPnet, 2013

Inflation source: Inflation of 3.6% (2015 to June 2016), [US Bureau of Labor Statistics]

Note: Non-reported assumed to be at 0% prevalence

Mortality costs

Table S10. Summary mortality related costs (all patients)

Drug	Mortality	Average costs
Eltrombopag	0.1%	44.01
Romiplostim	0.1%	72.85
Watch and rescue	0.2%	127.76