The Budget Impact of Cangrelor for the Treatment of Patients Undergoing Percutaneous Coronary Intervention when oral $P2Y_{12}$ Inhibitors are not Feasible or Desirable in the UK

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Background

- ST-segment elevation myocardial infarction (STEMI) is a type of coronary artery disease (CAD) characterised by occlusion of one or more coronary arteries, leading to myocardial ischaemia, followed by myocardial injury or death.[1]
- STEMI patients undergoing percutaneous coronary intervention (PCI) are offered antiplatelet therapies to reduce the risk of myocardial ischaemic events, particularly stent thrombosis.[2]
- Cangrelor is indicated for the reduction of the rate of thrombotic cardiovascular events in patients with CAD undergoing PCI, who have not received an oral $P2Y_{12}$ inhibitor prior to the PCI procedure, and in whom oral therapy with $P2Y_{12}$ inhibitors is not feasible or desirable.[3]
- The pooled analysis of the CHAMPION clinical trials programme evaluating the efficacy and safety of cangrelor vs clopidogrel reported that cangrelor significantly reduced the odds of the primary efficacy composite of all-cause death, myocardial infarction, ischaemia-driven revascularisation, or stent thrombosis at 48h by 19% (p = 0.0007 vs. clopidogrel), and stent thrombosis (key secondary endpoint) by 41% (p = 0.0008 vs. clopidogrel).[4]

Objective

- The objective of this analysis is to estimate the UK budget impact of introducing cangrelor for the STEMI population in whom oral $P2Y_{12}$ inhibitors are not feasible or desirable.

Methods

- Efficacy (thrombotic events), safety (bleeding events), and cost data were based on clinical trials, literature and the British National Formulary (Table 1 and Table 2). Efficacy data for cangrelor and clopidogrel was sourced from a pooled analysis of the CHAMPION clinical trials programme.[4] Efficacy data for prasugrel and ticagrelor in comparison to clopidogrel was sourced from a network meta-analysis of 15 randomised controlled trials by Westman et al.[5] Efficacy data for eptifibatide and tirofiban was sourced from a pooled analysis of the CHAMPION clinical trials programme, using a subgroup patients receiving routine GPIs.[6] The efficacy of aspirin plus heparin was conservatively assumed to be equal to clopidogrel since efficacy data for aspirin and heparin alone is limited.

Table 1: Efficacy and safety data used in the budget impact model

	Efficacy outcomes at 48 hours of PCI				Safety outcomes, TIMI, at 48 hours of PCI		Reference
	ST	MI	IDR	Death	Major	Minor	
Cangrelor	0.50%	3.11%	0.53%	0.26%	0.25%	0.61%	4
Base case comparators							
Eptifibatide	0.60%	2.40%	0.80%	0.40%	0.80%	1.60%	6
Tirofiban	0.60%	2.40%	0.80%	0.40%	0.80%	1.60%	
Aspirin & heparin*	0.85%	3.65%	0.74%	0.36%	0.22%	0.41%	4
Scenario analysis comparators							
Clopidogrel	0.85%	3.65%	0.74%	0.36%	0.22%	0.41%	4
Prasugrel	0.42%	2.77%	0.59%	0.36%	0.35%	0.44%	5
Ticagrelor	0.57%	2.74%	0.62%	0.34%	0.25%	0.65%	

*Efficacy assumed to be equal to clopidogrel - a conservative assumption that favours aspirin and heparin.

Table 2: Cost data used in the budget impact model

Event	Cost per event	Reference
Clinical events		
Ischaemic events*		
ST	£295.99	8
MI	£295.99	8
IDR	£295.99	8
Bleeding events**		
Major	£366.35	9
Minor	£366.35	9
Cardiac death	£0.00	10
Antiplatelet therapy†		
Cangrelor	£250.00	11
Oral $P2Y_{12}$ inhibitors		
Clopidogrel	£0.20	12,13
Prasugrel	£1.09	14,15
Ticagrelor	£1.95	16,17
Routine GPIs‡		
Eptifibatide	£128.37	18,19
Tirofiban	£292.22	20,21
Aspirin	£0.04	22,23
Hospital stay cost		
Post-operative day in hospital	£478.78	24

- Length of stay data for PCI using comparator therapies was sourced from Hospital Episode Statistics (HES) data.[7] Post-operative stay for comparators was calculated as the mean length of stay for non-elective PCI minus the mean pre-operative length of stay. Post-operative length of stay data for cangrelor was calculated by applying the percentage reduction in clinical events (ischaemic events, bleeding events and cardiac death) for cangrelor compared to weighted comparator therapies (19.88% reduction).[4–6] Length of stay for PCI using comparator therapies was therefore estimated at 3.59 days and length of stay for PCI using cangrelor was estimated at 2.88 days.
- Comparators in the base case were glycoprotein IIb/IIIa inhibitors (GPIs) (eptifibatide and tirofiban), and aspirin and heparin alone, reflecting expected use of cangrelor in UK centres for this population, following advice from UK clinicians.
- A scenario analysis was carried out which compared cangrelor to oral $P2Y_{12}$ inhibitors (clopidogrel, prasugrel, ticagrelor) and tirofiban.
- Cangrelor uptake was conservatively estimated as 10%, 30%, 50%, 70% and 90% in years 1-5, respectively. These values can be amended following local formulary discussions.

*All costs assumed to be equal to the cost of myocardial infarction based on the approach by Lizano-Díez and Paz Ruiz.[10] Hospitalisation accounted for 95% of ischaemic event costs.[8]
**Major and minor bleeding costs assumed to be equal based on the approach by Lizano-Díez and Paz Ruiz.[10]
†All drug costs calculated for an average 70kg adult. There are no additional administration costs. Heparin costs are excluded as assumed to be equal in all treatment arms.
‡GPI infusion is assumed to be 24 hours based on SmPC.[19,21] Split between eptifibatide and tirofiban for bailout GPI use is assumed to be equal. Bailout GPI dose is assumed to be equal to routine GPI dose.

Results

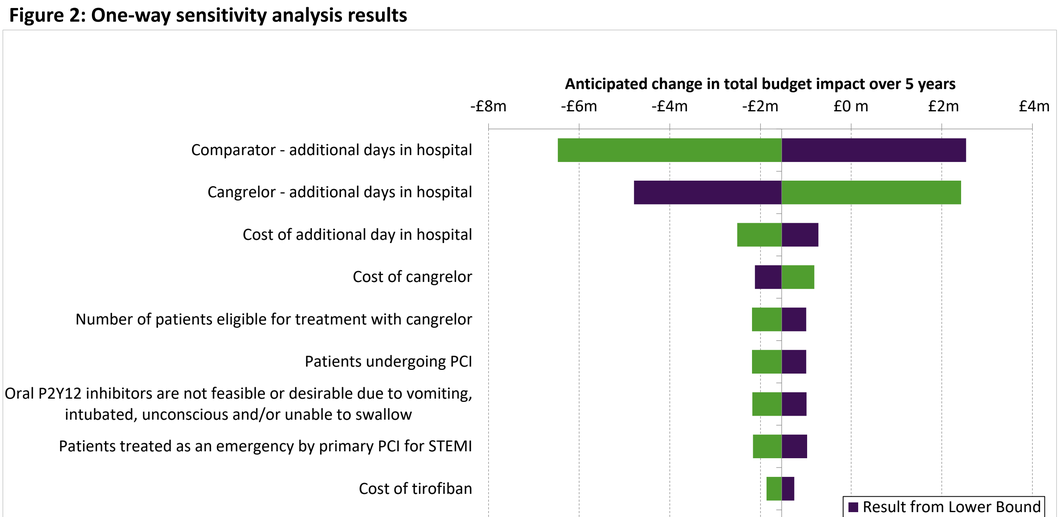
Base case

- The cangrelor-eligible population was estimated at 2,683 patients per year based on the National Audit of PCI 2021 and clinical expert advice.[25] 100,112 PCI procedures were performed in 2019/20, of which 26.8% were treated as an emergency by primary PCI for STEMI. Oral $P2Y_{12}$ inhibitors are not feasible or desirable in an estimated 12.5% of patients, as validated by clinician input.
- Over 5 years, cangrelor leads to a cost saving of £1,531,266 (-6.07%), varying from £64,918 (-1.29%) in year 1 to £547,588 (-10.85%) in year 5. A total of 4,785 hospital days and 76 clinical events are predicted to be avoided. The reduction in hospital days is driven by a reduction in ischaemic events (ST, MI and IDR).
- Tabulated results are available in Table 3. Figure 1 and Figure 2 display the total budget impact over 5 years and the annual budget impact, respectively.

Table 3: Budget impact summary results

	Total over 5 years	Average over 5 years
Patients eligible for treatment	13,415	2,683
Patients treated with cangrelor	6,708	1,342
Total costs in scenario without cangrelor	£25,234,927	£5,046,985
Total costs in scenario with cangrelor	£23,703,661	£4,740,732
Net budget impact (£)	-£1,531,266	-£306,253

Figure 1: Annual and total 5-year budget impact of introducing cangrelor to the market



Scenario analysis

- In the scenario including oral $P2Y_{12}$ inhibitors and tirofiban, the cangrelor-eligible population was estimated to be the same as the base case.
- Over 5 years, cangrelor leads to a modest cost increase of £1,102,586.43 (+4.62%), varying from £40,436 (+0.85%) in year 1 to £400,599 (+8.40%) in year 5.
- Over 5 years the total costs in the scenario with cangrelor increase by 5.27% compared to the base case.
- Over 5 years, a total of 729 hospital days are predicted to be avoided and one clinical event is predicted to be avoided. The reduction in hospital days is driven by a reduction in ischaemic events.

One-way sensitivity analysis

- A one-way sensitivity analysis (OWSA) was carried out to test parameter uncertainty. Parameters were varied by upper and lower confidence intervals, or ±20% in the absence of these data (Figure 2).
- OWSA results are centred on the base case total net budget impact, -£1,531,266. The model was most sensitive to additional days in hospital for cangrelor and the comparator therapies and the cost of cangrelor.

Figure 2: One-way sensitivity analysis results

Discussion

- This model demonstrates that introducing cangrelor in the UK may lead to cost savings and a reduction in hospital stays.
- Limitations in the present budget impact model include:
  - The efficacy of aspirin and heparin was assumed to be equal to clopidogrel. This is likely to be a conservative assumption that favours aspirin and heparin.
  - Market share of cangrelor and its comparators may differ from the model assumptions in forthcoming years. If cangrelor uptake is greater than estimated here, cost savings may be higher than in the base case analysis.
  - The same cost for major bleeding events and minor bleeding events was used due to lack of data. Therefore, bleeding costs may have been overestimated.
  - The cost for stent thrombosis and ischaemia-driven revascularisation were assumed to be the same as myocardial infarction due to lack of data availability. It is anticipated that a stent thrombosis or ischaemia-driven revascularisation would lead to an additional PCI procedure. Therefore, it is likely that this is a conservative assumption.

Conclusion

- Cangrelor represents an alternative therapy for the treatment of the STEMI population in whom oral $P2Y_{12}$ inhibitors are not feasible or desirable.
- Over 5 years, the introduction of cangrelor is estimated to lead to a cost saving of £1,531,266 (-6.07%).
- Introducing cangrelor in patients undergoing PCI for STEMI when oral $P2Y_{12}$ inhibitors are not feasible or desirable may lead to cost savings in the UK driven by a reduction in complications leading to reduced hospital activity.

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Abbreviations

CAD – coronary artery disease; GPI – glycoprotein IIb/IIIa inhibitor; HES – Hospital Episode Statistics; IDR – ischaemia-driven revascularisation; MI – myocardial infarction; OWSA – one-way sensitivity analysis; PCI – percutaneous coronary intervention; ST – stent thrombosis; STEMI – ST-segment elevation myocardial infarction; TIMI – Thrombolysis in myocardial infarction.

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