NICE advice

ClearWay RX for drug delivery to coronary artery thrombotic lesions

Medtech innovation briefing
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Summary

The ClearWay RX is a rapid exchange perfusion catheter for localised delivery of diagnostic or therapeutic agents, including drugs such as abciximab to dissolve blood clots in coronary arteries. The relevant evidence for this indication is very limited in quantity and comes from 2 small randomised controlled trials (1 available only as a conference presentation) which were inadequately or not powered to detect important differences in clinical outcomes. The published COCTAIL trial showed no significant difference in the primary outcome (thrombus score) but improvement in some outcomes for patients having abciximab using ClearWay RX compared with guide catheter or intravenous administration. These included the extent of stenosis, thrombolysis in myocardial infarction frame count, procedure-related myocardial infarctions and major adverse coronary events at 1 year. The list price of a single ClearWay RX unit is £600 excluding VAT.

Note that administering drugs such as abciximab using ClearWay RX may be outside their UK marketing authorisation.

Product summary and likely place in therapy	Effectiveness and safety
• The ClearWay RX is a rapid exchange perfusion balloon catheter, made from expanded polytetrafluoroethylene, for localised delivery of diagnostic or therapeutic agents including drugs. • This briefing evaluates its use for delivering abciximab to dissolve blood clots in coronary arteries, following episodes of unstable angina or myocardial infarction. It would replace standard delivery routes for the same drug, including intravenous or intracoronary administration, in patients for whom it is suitable.	• The relevant evidence summarised in this briefing is very limited in quantity and comes from 2 randomised controlled trials including a total of 98 patients. Both trials evaluated patients with unstable angina or myocardial infarction and compared abciximab delivered into the coronary artery using the ClearWay RX catheter with guide catheter (COCTAIL), or intravenous delivery (Crystal AMI). • In the COCTAIL trial (n=50), there was no statistically significant difference in the primary outcome (thrombus score) with ClearWay RX compared with guide catheter delivery of abciximab. There was a statistically significant improvement in the extent of stenosis of the target artery, coronary blood flow as measured by the thrombolysis in myocardial infarction frame count (TIMI), procedure-related myocardial infarctions and major adverse cardiac events at 1 year with ClearWay RX. There was no significant difference between the 2 groups in myocardial blush grade (a measure of myocardial reperfusion) or in the number of target vessel revascularisations. However, the study was not powered adequately to detect important differences in clinical outcomes, included patients with a range of acute coronary syndromes, and did not assess long-term clinical outcomes. It was not designed to distinguish between the thrombolytic action of abciximab and the physical displacement of the thrombus using ClearWay RX.

	• The Crystal AMI trial (n=48) is reported as a conference presentation only and has not been peer-reviewed. The trial showed improvements in some outcomes for patients having ClearWay RX compared with patients having guide catheter but the report is lacking in detail and the trial is described as a proof-of-concept study which was not powered to detect statistically significant differences in clinical outcomes.
Technical and patient factors • The ClearWay RX's semi-compliant balloon design and atraumatic tip support its use in target vessels while reducing the potential for additional vessel trauma. • The ClearWay RX catheter is narrow (0.014" guidewire compatible), allowing it to be used during routine angioplasty. It allows for much higher local drug concentration than intravenous administration. • It is intended for use by interventional cardiologists trained in percutaneous interventional techniques, in settings such as cardiac catheterisation units. • There is currently a US Food and Drug Administration (FDA) consent decree applying to the ClearWay RX balloon catheter. • Administering drugs such as abciximab using ClearWay RX may be outside their UK marketing authorisation.	**Cost and resource use** • The list price of 1 ClearWay RX unit is £600 excluding VAT. • No published evidence on resource consequences was identified.

Introduction

Coronary heart disease (CHD) is the leading cause of death in the UK, responsible for more than 73,000 deaths each year. It is estimated that 2.3 million people are living with CHD in the UK – over 1.4 million men and 850,000 women. The incidence of CHD increases with age and it is more common in people with type 1 or type 2 diabetes, high blood pressure or high cholesterol and in those who smoke (British Heart Foundation 2015).

CHD is characterised by narrowing (stenosis) of the coronary arteries caused by the development of an atherosclerotic plaque, which consists of fat, cholesterol and other blood-borne substances. Atherosclerotic plaques may be stable, often causing no symptoms, or unstable where the material inside the plaque may be exposed to the circulation. This can lead to blood clots forming in the arteries, reducing blood flow and consequently oxygen supply to the heart.

Acute coronary syndrome refers to a group of acute conditions caused by the sudden reduction in the oxygen supply to the heart muscle. This can trigger a myocardial infarction (MI), which may result in long-term heart muscle dysfunction and death. There are 3 main types of acute coronary syndrome:

- ST-elevation myocardial infarction (STEMI) in which the vessel is completely occluded, which can cause extensive damage to a large area of the heart
- non-ST-elevation myocardial infarction (NSTEMI) in which the blood vessel is partially occluded, resulting in damage to a smaller area of the heart
- unstable angina, in which the blood flow is restricted but there is no permanent damage to the heart.

Percutaneous coronary intervention (PCI) is a procedure used to widen the coronary artery. NSTEMI and STEMI account for 65% and 35% of respective cases of acute coronary syndromes where PCIs are performed (British Cardiovascular Intervention Society 2013). Myocardial infarction is associated with the formation of blood clots (unstable angina tends not to be, so is outside the scope of this briefing). In NSTEMI, and after opening the artery in STEMI, dislodged blood clots can lead to downstream microvascular impairment and the no-reflow phenomenon, where blood flow to the ischaemic tissue may still be impeded even after the blockage is removed. This is caused by platelet-fibrin aggregates in the distal arterial bed, which stimulate an inflammatory cascade that can perpetuate myocardial oedema, vessel spasm and endothelial dysfunction.

Technology overview

This briefing describes the regulated use of the technology for the indication specified, in the setting described, and with any other specific equipment referred to. It is the responsibility of healthcare professionals to check the regulatory status of any intended use of the technology in other indications and settings. Readers should note that administering drugs such as abciximab using ClearWay RX may be outside their UK marketing authorisation.

About the technology

CE marking

Atrium Medical, part of the Atrium Maquet Getinge group, received a CE mark for the ClearWay RX in March 2010. It is a class III medical device.

Description

The ClearWay RX is a rapid exchange perfusion balloon catheter for localised delivery of diagnostic or therapeutic agents within coronary or peripheral vessels. It is a low pressure catheter which incorporates a thin, semi-compliant microporous PTFE balloon material. It allows for selective and controlled infusion of therapeutic drugs at very low pressures. The catheter is narrow (0.014" guidewire compatible), allowing access consistent with routine PCI practice, and is compatible with 6–7 Fr guide catheters (depending on the size of the balloon). Radiopaque markers are located within the balloon treatment zone to assist in catheter placement under fluoroscopy. The ClearWay RX catheter is available in 1.0–4.0 mm balloon diameters and in balloon lengths of 10–50 mm. Longer balloons allow a larger blood clot to be treated in a single procedure, and are used in coronary artery bypass grafts.

The ClearWay RX balloon has an atraumatic tip, which is intended to reduce the potential for additional damage to diseased vessels. The catheter is designed to optimise drug delivery by occluding blood flow and infusing the drug directly at the site of the stenosis. These combined actions are designed to allow the drug to be delivered with minimal dilution and to increase drug residence time while the balloon is inflated. This results in a higher localised drug concentration compared with intravenous delivery, without increasing systemic load beyond the initial bolus delivered, with the intention of limiting adverse events such as bleeding complications.

Setting and intended use

ClearWay RX is indicated for use by interventional cardiologists trained in surgical, angiographic and PCI techniques, in specialised settings such as catheterisation labs in coronary care units. Standard visualisation procedures would be used, such as X-ray fluoroscopy.

ClearWay RX is only intended to be used for the localised perfusion of various diagnostic and therapeutic agents into the coronary (and peripheral) vasculature. It is not intended for use in percutaneous transluminal angioplasty or stent deployment, or in the neurovasculature. The scope of this briefing is the delivery of thrombolytic drugs to coronary arteries.

Current NHS options

After addressing risk factors (for example smoking, hyperlipidaemia, obesity and hyperglycaemia), symptoms of a blocked artery may be treated with beta-adrenergic blockers, nitrates, calcium-channel blockers, antiplatelet agents and statins. If medical management fails or is inappropriate, the usual options are surgical coronary artery bypass grafting or percutaneous transluminal coronary angioplasty, usually involving a bare metal or drug-eluting stent inserted where the vessel is stenotic. In recent years, filters and aspiration devices, as well as drug strategies such as glycoprotein IIb/IIIa inhibitors, have been tested to prevent thrombus micro-embolisation. The drugs can be given intravenously or via the coronary arteries using a coronary catheter.

Other drug-eluting balloon catheters are available and in use in the NHS (Waksman and Pakala 2009). NICE is aware of the following CE-marked device that appears to fulfil a similar function to the ClearWay RX:

- GENIE local drug delivery catheter (Acrostak Corporation).

Costs and use of the technology

The list price of 1 ClearWay RX balloon catheter is £600 excluding VAT. A guidewire is needed to deliver the device, but because a guidewire would be needed for a PCI anyway, the cost is not included here. ClearWay RX balloon catheters are single use but can be used several times in the same patient during a single procedure.

Likely place in therapy

The ClearWay RX would be used in hospital patients having angiographic procedures to aid in the dissolution of blood clots in coronary arteries that are continuing to cause symptoms and may

cause further myocardial damage, following acute coronary syndrome events. It can also be used in cases of no-reflow through the coronary artery. It would be used as an alternative to systemic administration of the therapeutic agents which are intended to break down the clot.

Specialist commentator comments

All 3 specialist commentators noted that there is limited evidence to support the use of ClearWay RX. One specialist commentator said that it is possible that any reduction in blood clot burden with ClearWay RX may have been a result of physical displacement, pushing clot fragments distally away from the lesion. Demonstrating this point, there is no evidence of the ClearWay RX using abciximab compared with the ClearWay RX using saline.

Two specialist commentators said that the Infuse AMI trial has often been quoted as good evidence for the effectiveness of ClearWay RX, but the trial does not provide information on the comparative effectiveness of different routes of drug administration.

One specialist commentator stated that, with a reduction in the routine use of thrombectomy (clot aspiration) following the TASTE and TOTAL trials, and a reduction in use of the intravenous anticoagulant bivalirudin following the HEAT-PPCI trial, the incidence of residual blood clots may rise, increasing the need for alternative strategies such as ClearWay RX. However, they also noted that residual blood clots are relatively uncommon, and alternative methods of dissolving them already exist (such as administering the agent directly into the coronary artery using a guide catheter or giving the agent intravenously).

One specialist commentator noted that it can be difficult to deliver drugs into a vessel where no-reflow is present and that ClearWay RX can be used for this. They did, however, state that it is often better to give glycoprotein inhibitors to patients at risk before no-reflow develops.

One specialist commentator stated that it is currently unclear whether reducing blood clot burden, or even an improvement in microvascular perfusion or myocardial blush grade, translates into favourable clinical outcome. This is demonstrated by a recent systematic review of thrombectomy compared with no intervention in STEMI (Elgendy et al. 2015).

One specialist commentator stated that the cost of 1 ClearWay RX catheter is equivalent to the cost of multiple angioplasty balloon catheters.

Equality considerations

NICE is committed to promoting equality, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others. In producing guidance, NICE aims to comply fully with all legal obligations to:

- promote race and disability equality and equality of opportunity between men and women
- eliminate unlawful discrimination on grounds of race, disability, age, sex, gender reassignment, marriage and civil partnership, pregnancy and maternity (including women post-delivery), sexual orientation, and religion or belief (these are protected characteristics under the Equality Act 2010).

Coronary heart disease is more common in people over the age of 65 years and affects more men than women. Age and sex are protected characteristics under the Equality Act 2010.

Evidence review

Clinical and technical evidence

Regulatory bodies

A search of the Medicines and Healthcare Products Regulatory Agency website identified a Consent Decree issued by the US Food and Drug Administration (FDA) for medical devices supplied by Atrium Medical. This applies to the ClearWay RX (Medicines and Healthcare products Regulatory Agency 2015). The FDA has identified problems with quality management systems at Maquet and its subsidiaries (including Atrium Medical). The consent decree requires that Atrium Medical's (Maquet) customers sign a Certificate of Medical Necessity to allow the company to continue supplying these medical devices.

A search of the FDA Manufacturer and User Device Facility Experience database identified 22 records of adverse events related to the ClearWay RX. Some of these followed its use in peripheral vasculature, where the original injury resulted in amputation, and some were associated with the Infuse AMI trial (described in the clinical evidence section). Some of the reports indicate that major acute coronary events (MACE) have occurred when using the device, including cardiac arrest, but causation is unclear. Other events include renal failure, leakage of drug between the balloon and the guidewire, and mechanical problems.

Clinical evidence

Eighteen studies of potential relevance to the ClearWay RX perfusion balloon catheter were identified, of which 16 were excluded from further assessment:

- One study compared intracoronary delivery of eptifibatide via a ClearWay RX catheter with thrombus aspiration using a different type of catheter (Hamza et al. 2014). This was excluded as neither of the control groups had eptifibatide, so any observed effectiveness in the ClearWay RX arm would be confounded by the use of the drug.
- There were 11 non-comparative studies (case series) investigating the use of the ClearWay RX to deliver a variety of drugs. However, because there were no comparison groups, these have also been excluded because it would not be possible to distinguish the effect of ClearWay RX from that of the drug it was delivering. In addition, there were 3 randomised control trials listed on the manufacturer's website that had no mention of the use of the ClearWay RX (Svilaas et al. 2008, Thiele et al. 2008, Zhao et al. 1999).
- The Infuse AMI trial (Gibson et al. 2011, Stone et al. 2013, 2012, Tomey et al. 2015) was a large randomised controlled trial with 4 arms. The objective of the trial was to demonstrate that administrating an intracoronary bolus of abciximab before stent implantation in patients with anterior STEMI results in reduced infarct size compared with no abciximab bolus. The 4 arms were:
    - aspiration of the thrombus (blood clot) plus intralesional abciximab (0.25 mg/kg) delivered using a ClearWay RX catheter
    - aspiration of the thrombus with no intralesional abciximab
    - no aspiration of the thrombus but with intralesional abciximab (0.25 mg/kg) delivered using a ClearWay RX catheter
    - no aspiration of thrombus with no intralesional abciximab.

This study was excluded because it does not allow for the comparison of intralesional abciximab delivered by a ClearWay RX catheter with drug delivery by another means.

Two comparative studies (COCTAIL [Prati et al. 2010, 2011] and Crystal AMI trial [Dave 2010]) were identified on the use of the ClearWay RX in coronary arteries and are included in this briefing.

COCTAIL was a randomised controlled trial that took place in coronary care units in Rome and Catania in Italy and Warsaw in Poland (see table 1 for characteristics of the trial). The trial aimed to

investigate whether local abciximab delivery to the site of an intracoronary thrombus is more effective than intracoronary bolus infusion in patients with acute coronary syndromes having PCI and downstream clopidogrel administration. The trial included patients with unstable angina, NSTEMI and STEMI having primary PCIs, with a significant lesion in the culprit artery indicative of local thrombus (thrombus score ≥50 according to optical coherence tomography [OCT]). The intervention was abciximab (0.25 mg/kg) given through a ClearWay RX catheter, compared with the same dose of abciximab given through a guide catheter. The primary outcome measure was a change in thrombus burden, as defined by the thrombus score. This was based on the semi-quantitative assessment of thrombus (number of involved quadrants in the cross-sectional OCT images) and the longitudinal extension of the thrombus. Other outcomes included arterial profile, thrombus scores, myocardial blush grade, thrombolysis in myocardial infarction (TIMI) frame count, and clinical events at 30 days and 1 year. The sample size was 50 patients, with 25 in the ClearWay RX arm and 25 in the control arm. There were no differences in the baseline characteristics between the 2 groups including demographic or previous medical history factors. The results showed no significant differences between the 2 groups for the primary outcome measure of thrombus score (ClearWay RX group mean score 68.8 (standard deviation [SD] 44.8), control group mean score 85.4 (SD 52.7, p=0.393). However, there were statistically significant improvements for the ClearWay RX group in the extent of stenosis of the target artery, TIMI frame count, procedure-related myocardial infarctions and major adverse coronary events at 1 year (see table 2). There were no statistically significant differences between the 2 groups in mean myocardial blush grade and the number of target lesion revascularisations at 1 year. The authors concluded that local intracoronary delivery of abciximab through a ClearWay RX catheter markedly reduces thrombus burden, with the potential to improve coronary microcirculation and reduce major event rates.

The Crystal AMI trial (Dave 2010) was reported in a conference presentation only and does not appear to have been published. The lead author was contacted but no further information was available. Crystal AMI was described as a proof-of-concept trial that was not powered to show statistical differences. It was a single-centre randomised controlled trial in patients with STEMI within 6 hours of symptom onset (see table 3). The intervention was intracoronary abciximab via a ClearWay RX catheter and control was intravenous abciximab. Follow-up was to 30 days. The primary outcome was TIMI myocardial blush grade, and other outcomes included TIMI flow, ST resolution, left ventricular function at hospital discharge, readmissions and deaths. The results for TIMI myocardial blush grade >2 were 92% in the intervention group and 87% in the control group. No statistical significance estimates were given so it is unclear whether any of the outcomes were statistically significantly different. The author's conclusions were that intracoronary abciximab via a ClearWay RX catheter is safe and effective, and produced higher myocardial blush grade scores and a trend towards higher ST-segment resolution.

Recent and ongoing studies

One ongoing trial on the ClearWay RX for coronary artery thrombus dissolution was identified. The protocol for this study is published (Prati et al. 2013) and 2 abstracts with results were found (Gatto et al. 2014a, 2014b). Neither of the abstracts gave results attributable to the intervention group.

Costs and resource consequences

No published evidence on resource consequences was identified.

Strengths and limitations of the evidence

In the COCTAIL trial (Prati et al. 2010, 2011), a clear hypothesis was evaluated in terms of the patients included, and the intervention and control used. The randomisation schedule was devised and implemented by the study statistician. It was an open-label trial so there was no allocation concealment. Patients were analysed in the groups to which they were assigned, but not all patients were accounted for in the outcomes assessment (5 were excluded from the ClearWay RX group and 4 from the control group). However, reasons for exclusion were given. In the ClearWay RX group, the reasons were insufficient OCT image quality (n=3), wrong segment matching (n=1) and thrombus score >50 (n=1). In the control group the reasons were insufficient image quality (n=3) and wrong segment matching (n=1). It would have been very difficult to blind the investigators because of the use of different equipment in the 2 groups during the procedure. There was no mention of blinding of patients or outcome assessors. The 2 groups were similar at the start of the trial for a wide variety of potentially confounding factors, and except for the interventions it appears that both groups were treated in a similar way. The sample size calculation estimated that 40 patients would need to be enrolled to achieve a 25% difference in the primary end point. This is a large difference and was not seen in the results. It is likely that a small difference would not be seen, so a suitably powered trial would need to include several hundred patients. The patients in the trial were from 2 European countries so the results are likely to be generalisable to patients treated within the NHS.

The Crystal AMI trial (Dave 2010) is reported only as a conference presentation so there are very few details about how the trial was done. A clear question was evaluated in terms of the patients included, and the intervention and control used. No details of the method of randomisation are given and the presence of allocation concealment is unclear. It is assumed that follow-up was completed and that patients were analysed in the groups to which they were randomised. It would be very difficult to blind the investigators because of the use of different equipment in the 2 groups

during the procedure. There was no mention of blinding of patients or outcome assessors. The 2 groups were similar at the start of the trial for a variety of potentially confounding factors such as age, gender, symptoms, prior intracoronary procedures, diabetes, smoking status and blood lipid profile. Apart from the interventions, it is unclear whether both groups were treated in a similar way. There was no sample size calculation given but the trial was described as a proof of concept that was not powered to show statistical differences, and no statistical significance estimates were given, so it is unclear whether any of the outcomes were statistically significantly different. Patients were from USA, so it is unclear if the results are generalisable to NHS practice.

Relevance to NICE guidance programmes

The use of ClearWay RX is not currently planned into any NICE guidance programme.

NICE has issued the following relevant guidance on a similar topic:

- SeQuent Please balloon catheter for in-stent coronary restenosis (2010) NICE medical technologies guidance 1

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Appendix

Contents

Data tables

Table 1 Overview of the COCTAIL trial (Prati et al. 2010, 2011)

Study component	Description
Objectives/ hypotheses	To investigate whether local abciximab delivery to the site of an intracoronary thrombus is more effective than intracoronary bolus infusion in patients with acute coronary syndromes undergoing percutaneous coronary intervention and downstream clopidogrel administration.

Study design	Randomised controlled trial
Intervention	Abciximab (0.25 mg/kg) given through a ClearWay RX catheter Comparator: Abciximab (0.25 mg/kg) given through a guiding catheter
Setting	Coronary care units in Rome and Catania in Italy and Warsaw, Poland. The date of the trial recruitment was not given but it is believed to be between 2001 (when the protocol was published) and 2010.
Inclusion/ exclusion criteria	Inclusion criteria: Patients with unstable angina, NSTEMI or STEMI undergoing primary PCI, with a significant lesion in the culprit artery indicative of local thrombus (thrombus score ≥50 according to OCT. Exclusion criteria: Myocardial ischaemia precipitated by a condition other than atherosclerotic disease, use of a fibrinolytic agent within 14 days before randomisation, use of abciximab or any other glycoprotein IIb/IIIa inhibitor within 30 days before randomisation, suspected active internal bleeding or history of haemorrhagic diathesis, major surgery, biopsy of a parenchymal organ, eye surgery or serious trauma, gastrointestinal or genitourinary bleeding of clinical significance within 6 weeks before randomisation, history of CVA or TIA within the previous 2 years or any CVA with a residual neurological deficit, administration of oral anticoagulants within 7 days before randomisation unless prothrombin time 1.2 or less times control (or international normalised ratio ≤ 1.4) or ongoing treatment with oral anticoagulant, known current platelet count < 100,000 cells/ µl, intracranial neoplasm, arteriovenous malformation, aneurysm or aneurysm repair, known allergy to abciximab or other murine proteins, known positive pregnancy test for women of childbearing age.
Primary outcomes	The primary outcome was change in thrombus burden defined by the thrombus score. This was assessed on the semi-quantitative assessment of thrombus (number of involved quadrants in the cross-sectional OCT images) and the longitudinal extension of the thrombus. Myocardial blush grade, TIMI frame count, arterial profile and clinical events at 30 days and 1 year were also measured.

Statistical methods	Categorical variables presented as counts and percentages and compared with chi-square or Fisher's exact tests. Continuous variables presented as mean±SD and compared with Student's t test.
Patients included	50 patients were included. ClearWay RX group: n=25, 72% men, mean age 62.7±9.2 years; 12% unstable angina, 48% NSTEMI, 40% STEMI. Control group: n=25, 68% men, mean age 64.4±10.3 years; 8% unstable angina, 56% NSTEMI, 36% STEMI. No difference in proportions with hypertension, diabetes mellitus, hyperlipidaemia, smoking, family history, prior MI, prior CABG, target vessel.
Results	See table 2
Author's conclusions	Local intracoronary delivery of abciximab through a ClearWay RX catheter significantly reduces thrombus burden, with the potential to improve coronary microcirculation and reduce major event rates.
Abbreviations: CABG, coronary artery bypass graft; CVA, cerebrovascular accident; MI. myocardial infarction; µl, microlitre; n, number of patients; NSTEMI, non-ST-elevated myocardial infarction; OCT, optical coherence tomography; SD, standard deviation; STEMI, ST-elevated myocardial infarction; TIA, transient ischaemic attack; TIMI, thrombolysis in myocardial infarction.	

Table 2 Summary of results from the Coctail trial (Prati et al. 2010, 2011)

	ClearWay	Control	Analysis
Randomised	n=25	n=25	
Efficacy	n=20	n=21	
Primary outcome: thrombus score (mean±SD)	68.8±44.8	85.4±52.7	p=0.393
Selected secondary outcomes:			
Diameter stenosis (%, mean±SD)	5.94±3.27	11.21±9.07	p=0.022
TIMI frame count (mean±SD)	15.3±10.2	21.1±9.9	p=0.049

Mean myocardial blush grade (%, mean±SD)	2.78±0.43	2.59±0.62	p=0.303
Clinical events at 30 days	0%	0%	Not applicable
Safety – procedure-related MI	10%	43%	p=0.018
MACE at 1 year	5.9%	27.2%	p=0.046
Target lesion revascularisation at 1 year	5.9%	21.6%	p=0.126
Abbreviations: MACE, major adverse coronary events; MI, myocardial infarction; n, number of patients; SD, standard deviation; TIMI, thrombolysis in myocardial infarction.			

Table 3 Overview of the Crystal AMI trial (Dave, 2010)

Study component	Description
Objectives/ hypotheses	To investigate whether delivery of intracoronary abciximab with ClearWay RX leads to better ST resolution, higher MBG, improved TIMI flow and smaller infarct size than intravenous abciximab during STEMI percutaneous coronary intervention.
Study design	Single-centre, prospective randomised controlled trial. Pilot proof-of-concept trial, not powered to show statistical differences. 30 day follow-up.
Intervention	Intracoronary abciximab given through a ClearWay RX catheter. Comparator: intravenous abciximab.
Setting	No information given.
Inclusion/ exclusion criteria	Inclusion criteria: Patients with STEMI, having PCI within 6 hours of symptom onset, and given heparin and 600 mg clopidogrel. No exclusion criteria were reported.
Outcomes	Primary: myocardial blush grade. Secondary: TIMI flow, ST resolution, LV function at discharge.
Patients included	50 patients were included, 48 were randomised. ClearWay RX group: n=25, 23 men, mean age 62±25 years. Control group: n=23, 18 men, mean age 65±23 years.

Results		
	Intracoronary abciximab through ClearWay RX	**Intravenous abciximab**
Primary outcome: Myocardial blush grade	Grade >2: 23/25 (92%) Grade 3: 18/25 (72%)	Grade >2: 20/23 (87%[a]) Grade 3: 12/23 (52%)
Selected secondary outcomes:		
TIMI flow	TIMI 0 flow: 1/25 TIMI 3 flow: 24/25 (96%)	TIMI 2 flow: 4/23 (96%) TIMI 3 flow: 19/25 (82%)
ST resolution	80% (21/25)	70% (18/23)
LV function at discharge	Not reported	Not reported
Readmissions	n=0	n=2
Safety – deaths	n=0	n=1
Author's conclusions	Intracoronary abciximab is safely and effectively delivered via ClearWay RX and produced higher MBG scores and a trend towards higher ST-segment resolution.	
Abbreviations: MBG, myocardial blush grade; PCI, percutaneous coronary intervention; STEMI, ST-elevated myocardial infarction. [a] Incorrectly reported as 86%.		

Search strategy and evidence selection

Search strategy

A. Database searches

Database: Ovid MEDLINE(R) <1946 to June Week 3 2015>

Search strategy:

1 ClearWay.mp. (23)

2 Cardiovascular Diseases/ or cardiovascular.mp. (368885)

3 catheter.mp. or Catheters/ (111731)

4 2 and 3 (3496)

5 limit 4 to (humans and yr="2005 -Current" and "therapy (maximizes specificity)") (83)

6 1 or 5 (106)

Database: Embase <1974 to 2015 30 June>

Search strategy:

1 peripheral infusion catheter/ (33)

2 ClearWay.mp. (70)

3 1 or 2 (93)

Database: Cochrane Library to 30 June 2015

Search strategy:

1 ClearWay (9)

B. Reference lists of reviews and other identified studies were checked to identify any further studies.

C. Information provided by the manufacturer for supporting this briefing report was also checked to identify any further studies.

D. The internet. Google Search: 30 June

Search Terms: ClearWay RX, Crystal AMI, Coctail, Libra AND coronary.

E. ClinicalTrials.gov, WHO ICTRP, and Current Controlled Trials were also searched for ongoing trials.

F. The manufacturer's website was thoroughly investigated.

Evidence selection

The inclusion criteria were as follows:

- **Patients:** adults with diffuse and multi-segment cardiovascular disease, particularly coronary artery. Patients with a thrombus occluding or narrowing an artery that needs to be cleared. Presentation could be STEMI or NSTEMI, vein grafts, no-reflow or slow flow, complex femoral popliteal occlusions, cases of critical limb ischaemia.
- **Intervention:** therapeutic drug delivery through the ClearWay RX balloon catheter. Drugs used include glycoprotein (GP) IIb/IIIa inhibitors (mostly) but also nitroglycerin, sodium nitroprusside, tPA, retevase, and paclitaxel.
- **Comparator(s):** drug delivery of the same drug using a sheath or guide catheter in the same artery, or injection of the same drug via a peripheral vein.
- **Outcomes:** any clinical, safety and resource use outcomes, such as removal of thrombus, restoration of blood flow, damage to artery wall, CVA, PE, thrombus relocation causing infarction.
- **Study design:** any controlled clinical studies including observational studies.

About this briefing

Medtech innovation briefings summarise the published evidence and information available for individual medical technologies. The briefings provide information to aid local decision-making by clinicians, managers and procurement professionals.

Medtech innovation briefings aim to present information and critically review the strengths and weaknesses of the relevant evidence, but contain no recommendations and **are not formal NICE guidance**.

Development of this briefing

This briefing was developed for NICE by Birmingham & Brunel External Assessment Centre. The interim process and methods statement sets out the process NICE uses to select topics, and how the briefings are developed, quality-assured and approved for publication.

Project team

- Birmingham and Brunel External Assessment Centre
- Medical Technologies Evaluation Programme, NICE

Peer reviewers and contributors

- Dr Catherine Meads, Reader in Health Technology Assessment, Brunel University
- Dr Carole Cummins, University of Birmingham

Specialist commentators

The following specialist commentators provided comments on a draft of this briefing:

- Dr Magdi El-Omar, Consultant Interventional Cardiologist, lead for the acute chest pain service and divisional lead for infection prevention and control, Manchester Heart Centre, Manchester Royal Infirmary
- Professor Anthony Gershlick, Consultant Cardiologist, University Hospitals of Leicester NHS Trust and Honorary Professor of Interventional Cardiology, University of Leicester
- Dr Stephen Hoole, Consultant Interventional Cardiologist and Interventional Research Lead, Papworth Hospital NHS Foundation Trust and Honorary Fellow, University of Cambridge

Declarations of interest

- Dr Magdi El-Omar received an honorarium approximately 3 years ago from Atrium (before they were taken over by Maquet) for a presentation on INFUSE-AMI at the EuroPCR conference in Paris.
- No other relevant interests were declared.

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