Use of cangrelor in percutaneous coronary interventions: a “new” weapon in the antithrombotic therapeutic armamentarium

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During the second half of 2019, cangrelor started selling in our country, a “new” antiplatelet drug with especial pharmacological properties that make it especially appealing for the management of certain clinical situations in the percutaneous coronary intervention (PCI) setting. The adjective “new” is in quotation marks because the clinical trial conducted proved its superiority compared to clopidogrel with ICP. The CHAMPION PHOENIX trial1 was published in 2013 and it was approved by regulatory authorities back in 2015. This delay has probably caused the scientific evidence to lose relevance and, in consequence this drug might not be widely accepted within the cardiology community. Also, the indication specified in the technical label is only based on the conditions of the clinical trial that prompted its approval—which is mandatory—not on real-world practices. This may be confusing when selecting those patients who may benefit from this drug.2

In short, cangrelor is an intravenous reversible, high-affinity antagonist of the platelet P2Y12 receptor of adenosine diphosphate to which it binds directly (without need for conversion into an active metabolite). In pharmacodynamic terms, the properties of cangrelor which it binds directly (without need for conversion into an active metabolite). In pharmacodynamic terms, the properties of cangrelor (more powerful and effective than clopidogrel and drugs of choice in patients with ACS). The second is that IP2Y12 pretreatment before the PCI was considered an exclusion criterion. We should remember that, although there are serious doubts about its pretreatment benefit in the ACS setting, especially in the non-ST-segment elevation acute coronary syndrome setting,9 this strategy is widely used in our country. As a matter of fact, the European technical label of this drug specifically says that cangrelor is indicated in association with acetylsalicylic acid in patients “who undergo PCI and have not received an oral P2Y12 inhibitor before the PCI, and in whom oral treatment with P2Y12 inhibitors is not possible or desired.”2 Still, the pharmacological properties of cangrelor make it especially interesting in situations where not only the aforementioned pretreatment has not occurred, but also in circumstances where it is considered insufficient. Proof of this is the experience published from the Swedish national registry (SCAAR) during the first 2 years of drug use that found an almost exclusive use of cangrelor in patients with STEMI who underwent primary percutaneous coronary intervention; in this real-world study, cangrelor was associated with a slightly higher risk of bleeding mainly at the cost of minor bleeding;4 this good safety profile is probably due to the fact that the drug is administered over a very limited span of time and its effect rapidly goes away after infusion.

The CHAMPION PHOENIX trial has received 2 important criticisms that may condition its implementation in our routine clinical practice. The first is that cangrelor was never compared to prasugrel or ticagrelor (more powerful and effective than clopidogrel and drugs of choice in patients with ACS). The second is that IP2Y12 pretreatment before the PCI was considered an exclusion criterion. We should remember that, although there are serious doubts about its pretreatment benefit in the ACS setting, especially in the non-ST-segment elevation acute coronary syndrome setting,9 this strategy is widely used in our country. As a matter of fact, the European technical label of this drug specifically says that cangrelor is indicated in association with acetylsalicylic acid in patients “who undergo PCI and have not received an oral P2Y12 inhibitor before the PCI, and in whom oral treatment with P2Y12 inhibitors is not possible or desired.”2 Still, the pharmacological properties of cangrelor make it especially interesting in situations where not only the aforementioned pretreatment has not occurred, but also in circumstances where it is considered insufficient. Proof of this is the experience published from the Swedish national registry (SCAAR) during the first 2 years of drug use that found an almost exclusive use of cangrelor in patients with STEMI who underwent primary percutaneous coronary intervention; in this real-world study, cangrelor was associated with a slightly higher risk of bleeding mainly at the cost of minor bleeding;4 this good safety profile is probably due to the fact that the drug is administered over a very limited span of time and its effect rapidly goes away after infusion.

The clinical development of cangrelor as a coadjuvant therapy in the PCI setting is based on the CHAMPION program, in which the first 2 studies conducted (CHAMPION PCI4 and CHAMPION PLATFORM5) were prematurely interrupted due to their futility, in part attributed to a restrictive definition of myocardial infarction.5,7 On the contrary, the CHAMPION PHORHORN clinical trial did prove the superiority of cangrelor vs clopidogrel reducing the main variable of efficacy [a composite of death, myocardial infarction, ischemia guided revascularization or stent thrombosis] after 48 hours in patients who underwent PCI to treat stable angina or any type of acute coronary syndrome (ACS) and who were not eligible for oral IP2Y12 pretreatment.1 We should mention that in a combined analysis of the 3 trials, cangrelor was associated with a slightly higher risk of bleeding mainly at the cost of minor bleeding;4 this good safety profile is probably due to the fact that the drug is administered over a very limited span of time and its effect rapidly goes away after infusion.

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The potential benefit of the drug for the prevention of intra-procedural thrombotic events should be weighed against the patient and procedural related bleeding risk

Figure 1. Potential favorable clinical settings for the use of cangrelor. ACS, acute coronary syndrome; CCS, chronic coronary syndrome; DAPT, dual antiplatelet therapy; iP2Y12, platelet P2Y12 receptor inhibitors; PCI, percutaneous coronary intervention; STEMI, ST-segment-elevation acute myocardial infarction.

The dose studied in the bridging therapy is an infusion of 0.75 µg/kg/min.

Taking all this into consideration, cangrelor should be primarily used in the cath lab in situations of periprocedural high thrombotic risk when oral iP2Y12 pretreatment has not occurred, is ill-advised or insufficient. The availability of the drug will probably not change our antiplatelet strategy radically in the short term in the PCI setting. However, in some situations (especially primary percutaneous coronary interventions) its particular pharmacological profile will be very useful. Therefore, its use will probably grow in the interventional cardiology community as we become more familiar with it. In conclusion, cangrelor is an interesting addition to our therapeutic armamentarium in the PCI setting because it can individualize and, therefore, optimize our antithrombotic strategy.

CONFLICTS OF INTEREST

J.L. Ferreiro has declared he has received funds for his lectures for Eli Lilly Co., Daiichi Sankyo Inc., AstraZeneca, Roche Diagnostics, Pfizer, Abbott, Boehringer Ingelheim, Bristol-Myers Squibb and Ferrer; also, he has received funds for his counselling for AstraZeneca, Eli Lilly Co., Ferrer, Boston Scientific, Pfizer, Boehringer Ingelheim, Daiichi Sankyo Inc., Bristol-Myers Squibb; he has also receive research grants from AstraZeneca. J.A. Gómez-Hospital has declared he has received funds for his counselling for Abbott, Medtronic, Boston Scientific, Terumo, and IHT.

REFERENCES


