

Supplemental Information

Direct intramyocardial injection

of VEGF mRNA in patients

undergoing coronary artery bypass grafting

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SUPPLEMENTARY TABLES

Table S1. Patient eligibility criteria.

Inclusion criteria
1. Provision of signed and dated informed consent before study procedures.
2a. Surgically sterile or using an acceptable method of contraception.
2b. Postmenopausal (amenorrhea for at least 12 months after cessation of all hormonal treatments and follicle-stimulating hormone levels in the postmenopausal range) or documented irreversible surgical sterilization (hysterectomy, bilateral oophorectomy, or bilateral salpingectomy).
3. Age of at least 18 years.
4. Enrollment at least 15 days before planned elective coronary artery bypass grafting surgery.
5. Moderately reduced global LVEF at rest ($30\% \leq \text{LVEF} \leq 50\%$) from medical records.
6. If on statin, angiotensin-converting enzyme inhibitor, angiotensin receptor blocker, or β -blocker, on a stable dose for at least 2 weeks before screening.
7. If a blood donor, agreement not to donate during the study and for 3 months following AZD8601 injection.
Exclusion criteria
1. Involvement in the planning and/or conduct of the study.
2. Previous randomization in the study.
3. Participation in another clinical study of an investigational product during the last 3 months.
4. Body mass index above 35 kg/m ² or poor image window for echocardiography.
5. Indication for emergency coronary artery bypass grafting (defined as significant worsening of coronary artery disease symptoms, such as crescendo angina, unstable angina, or acute coronary syndrome that requires rescheduling of the revascularization, or instability of symptoms during the 3 months before surgery).
6. History of ventricular arrhythmia (Lown grade III or higher) without an implantable cardiac defibrillator.
7. History of any clinically significant disease or disorder which, in the opinion of the investigator, may put the patient at risk, influence study results, or affect the patient's ability to participate.
8. Severe comorbidity that could interfere with the execution of the study or the interpretation of study results, or could affect the patient's safety, in the investigator's judgement.
9. Estimated glomerular filtration rate of 30 mL/minute or below (based on creatinine clearance assessed by local laboratory).
10. Contraindication for coronary flow velocity reserve or stress MBF assessments. ^a
11. Inability to comply with the protocol.
12. History of severe allergy or hypersensitivity or ongoing clinically important allergy or hypersensitivity to drugs with a similar chemical structure or class as the study drugs.
13. Unable to provide informed consent or communicate reliably with the investigator, or vulnerable (e.g. detained; protected under guardianship or trusteeship; committed to an institution).
14. Positive for hepatitis C virus antibody, hepatitis B virus surface antigen or hepatitis B virus core antibody or human immunodeficiency virus antibody at screening.
15. History of drug or alcohol abuse.
16. Current use of medications known to be associated with torsades de pointes.
17. History of QT prolongation associated with medication that required discontinuation of that medication.
18. Congenital long QT syndrome.
19. History of arrhythmia (multifocal premature ventricular contractions, bigeminy, trigeminy, ventricular tachycardia) that is symptomatic or requires treatment (CTCAE Grade 3).
20. Current atrial fibrillation or paroxysmal atrial fibrillation.

^a Known severe adverse reactions to adenosine, known elevated intracranial pressure, AV block worse than second degree or sick sinus syndrome in patients without pacemakers; verified echocardiographic heart rate below 40 beats per minute; systolic blood pressure below 90 mmHg; asthma or chronic obstructive pulmonary disease with a strong reactive component in the judgment of the investigator; dipyridamole, theophyllamine or fluvoxamine treatment that cannot be paused.

CTCAE, Common Terminology Criteria for Adverse Events; LVEF, left ventricular ejection fraction; MBF, myocardial blood flow.