



Title	A newly derived small synthetic compound alleviated ventricular fibrillation in a pig model with chronic myocardial infarction as revealed by optical mapping
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A correlation of mobilisation regimens and outcome during autologous haematopoietic stem cell mobilisation and transplantation

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Introduction: Autologous haematopoietic stem cell transplantation (ASCT) is the mainstay of treatment for plasma cell myeloma and selected cases of lymphoma. Haematopoietic stem cell (HSC) can be mobilised using combination of chemotherapy and granulocyte-colony stimulating factor (G-CSF). However it is associated with treatment toxicity and the need for prolonged hospitalisation. HSC can also be mobilised using G-CSF alone, but the yield may be lower. Plerixafor, a CXC chemokine receptor 4 (CXCR-4) antagonist, was recently approved by the US FDA in patients who failed G-CSF HSC mobilisation. In the present study, we compared the HSC yield and engraftment after ASCT in patients who underwent HSC mobilisation with these regimens.

Methods: Consecutive patients who underwent ASCT for plasma cell myeloma between 2009 and 2010 were retrospectively analysed. Total CD34⁺ cells collected, number of apheresis sessions and haematopoietic recovery after ASCT was correlated with their HSC mobilisation regimens. Numerical data were compared using Mann-Whitney *U* test and categorical data was evaluated using χ^2 test. A *P* value of less than 0.05 was considered statistically significant.

Results: A total of 28 patients were analysed; 18 patients have received cyclophosphamide (3 g/m²) and G-CSF for mobilisation (Cy+G-CSF), 10 received G-CSF of whom five required plerixafor (G-CSF+P) to achieve target cell dose of 2x10⁶/kg body weight. Patients receiving Cy+G-CSF required longer duration of hospitalisation when compared with G-CSF±Mozobil group. Most patients in the Cy+G-CSF group (n=15) required only one harvest whereas all patients in the G-CSF required more than one (*P*<0.01). There was no significant difference in neutrophil engraftment as well as hospital stay during ASCT in these patients.

Conclusion: The use of plerixafor improves the stem cell yield when added to G-CSF as mobilisation, and has a significant less hospital stay when compared with cyclophosphamide as mobilisation.

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A newly derived small synthetic compound alleviated ventricular fibrillation in a pig model with chronic myocardial infarction as revealed by optical mapping

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The electrophysiological hallmark of cells and tissues isolated from failing hearts is prolongation of action potential duration (APD), resulted from down-regulation of repolarising K⁺ currents and/or alterations in depolarising Na⁺ and Ca²⁺ currents, which predisposes the failing heart to lethal ventricular tachyarrhythmia (ventricular tachycardia [VT] and ventricular fibrillation [VF]). C11, a small synthetic Cl⁻ channel, exhibits membrane-repolarising power. Therefore, we hypothesise C11 corrects the delayed repolarisation and shortens APD at cellular level, thus modifying ventricular arrhythmogenic substrate at whole heart level. First, we demonstrated APD reduction upon C11 application (30 μM) at 37°C to isolated guinea pig ventricular cardiomyocytes with patch-clamp experiments in whole cell configuration (*Figure: upper panel*).

To examine whether C11 works in disease model, pig hearts with chronic myocardial infarction (MI) were optically mapped. Electrocardiograms (ECGs) [*Figure: middle panel*] and the optical mapping signals with optical timing maps [*Figure: lower panel*] displayed the attenuation of VF to VT in the presence of C11 (30 μM).

In conclusion, C11 alleviated VF in our ex-vivo pig heart model with chronic MI. Further investigation in the ionic properties of C11 will be worthy to further dissect the underlying mechanism of function posing potential use of C11 in clinical prospect.

