大阪大学 革新的医薬品・医療機器シーズ

オキシム誘導体徐放性マイクロスフェアー製剤（YS-1402）の重症心不全への適応

プロジェクト研究者名	医学系研究科 心臓血管外科学　教授　澤 芳樹、助教　福嶌 五月
	医学系研究科免疫再生制御学共同研究講座　特任准教授　宮川 繁

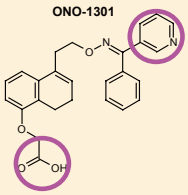
■プロジェクト概要

医師主導型治験 (Phase I/IIa)

目 的

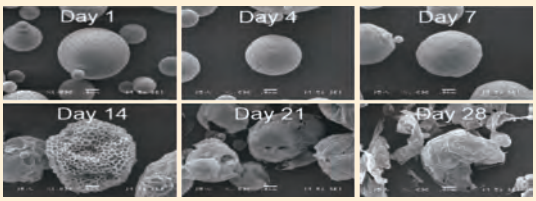
✓ 冠動脈バイパス手術を施行する虚血性心筋症患者に YS-1402 を単回心臓貼付投与した際の安全性、忍容性、有効性を検討する。
✓ 企業治験（Phase Ⅱ b/ Ⅲ）を経て、薬事承認・医薬品としての上市化を目指す。

オキシム誘導体；ONO-1301

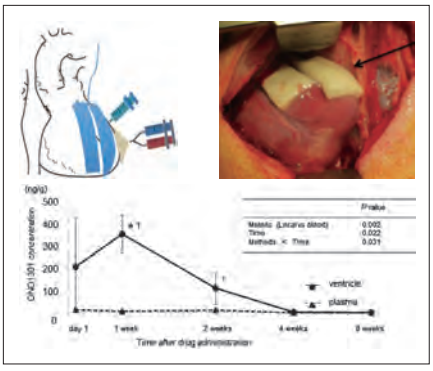


✓ Phase Ⅰ企業治験終了（抗血小板薬）
✓ プロスタグランジン IP 受容体作動
✓ トロンボキサン A2 合成酵素阻害
✓ 血管拡張・血管新生作用
✓ 抗炎症・抗線維化作用
✓ 速やかに肝代謝

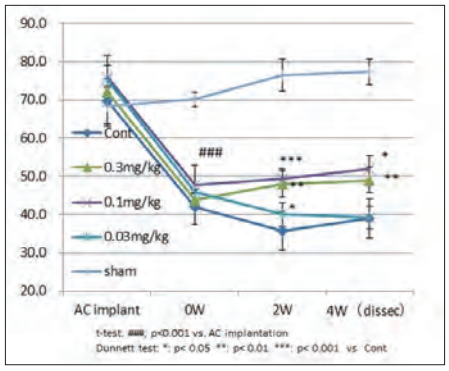
徐放性マイクロスフェアー；YS-1402



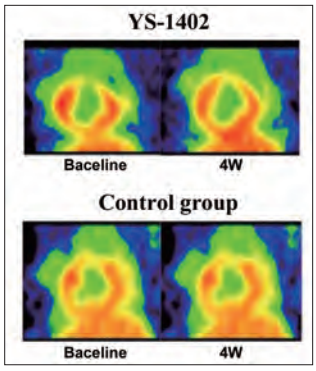
慢性心不全モデルを用いた YS-1402 製剤心臓貼付治療の前臨床試験



✓ 薬剤の心筋組織中濃度が 4 週間維持



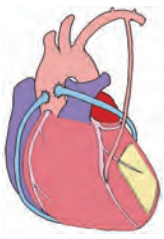
✓ YS-1402 投与量依存性に左室駆出率が向上



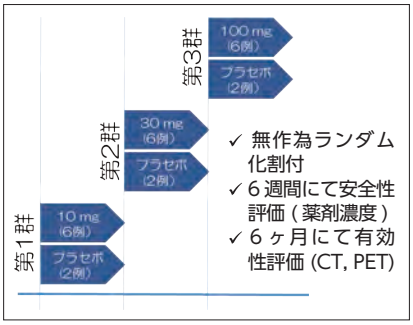
✓ 投与部位の血流向上

(Ishimaru et al. J Thorac Cardiovasc Surg 2013, Mizoguchi et al. AHA Scientific Sessions 2013 at Dallas)

プロトコール概要



✓ オンポンプ・オフポンプ
✓ 閉胸前に左室自由壁に貼付
✓ フィブリンスプレー



✓ 無作為ランダム化割付
✓ 6 週間にて安全性評価（薬剤濃度）
✓ 6 ヶ月にて有効性評価 (CT, PET)

【適応基準】
✓ 単独冠動脈バイパス術
✓ 心エコー検査で EF40% 以下
✓ 同意取得時に年齢が 20 歳以上

【除外基準】
✓ 不可逆的他臓器不全
✓ 悪性腫瘍
✓ 糖尿病性網膜症
✓ アルコール中毒・薬物依存
✓ 精神病・精神症状
✓ ゼラチン・アプロチニン過敏
✓ 他の治験終了後 6 か月以内

対 象 疾 患：重症虚血性心筋症
市　場　性：30 億円／年（国内 1 万人）
特 許 情 報：特許出願（企業との共同；計 5 報）
技術の特徴：セルフリーな新規体内誘導型再生治療剤

dmi Department of Medical Innovation, Osaka University Hospital
お問い合わせ
大阪大学医学部附属病院未来医療開発部
〒565-0871 大阪府吹田市山田丘2-2 Tel：06-6210-8289 Fax：06-6210-8301
e-mail：dmi@dmi.med.osaka-u.ac.jp URL：http://www.dmi.med.osaka-u.ac.jp

Seeds of innovative pharmaceuticals and medical devices from Osaka University

Slow-release microsphere of oxime derivative (YS-1402) for advanced cardiac failure

Investigators	Department of Cardiovascular Surgery, Graduate School of Medicine Professor Yoshiki SAWA, Assistant Professor Satsuki FUKUSHIMA
	Department of Immunology and Regenerative Medicine, Graduate School of Medicine Specially Appointed Associate Professor Shigeru MIYAGAWA

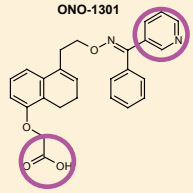
Project Outline

Investigator initiated clinical study (Phase I/IIa)

Objective

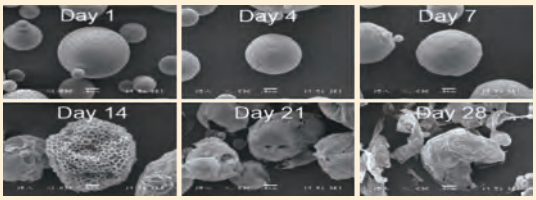
✓ To assess feasibility, safety and efficacy of epicardial placement of YS-1402 for patients undergoing coronary artery bypass grafting for ischaemic cardiomyopathy, towards pharmaceutical approval through subsequent Phase IIb/III study.

Oxime derivative; ONO-1301

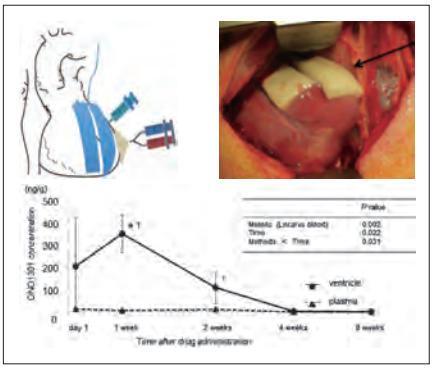


- ✓ Phase I study completed as antiplatelet drug
- ✓ Prostagrandin IP receptor agonist
- ✓ Thromboxan A2 synthase inhibition
- ✓ Vasodilation, Proangiogenesis
- ✓ Anti-inflammatory/fibrotic
- ✓ Rapidly degraded in the liver

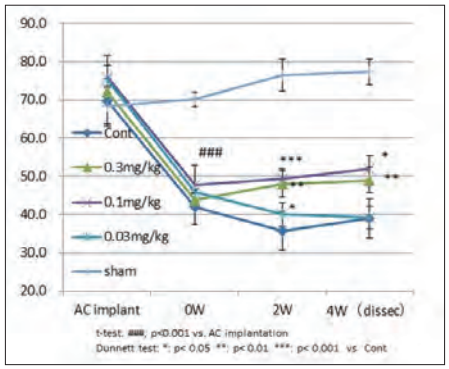
Slow-release microsphere; YS-1402



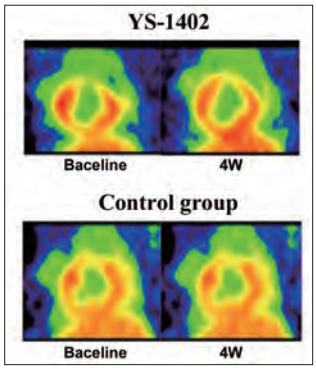
Preclinical study of YS-1402 treatment for ischaemic cardiomyopathy animal models



✓ Targeted drug delivery over 4 weeks



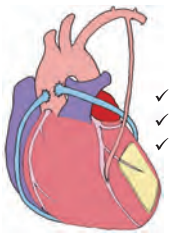
✓ Dose-dependent functional efficacy after the treatment



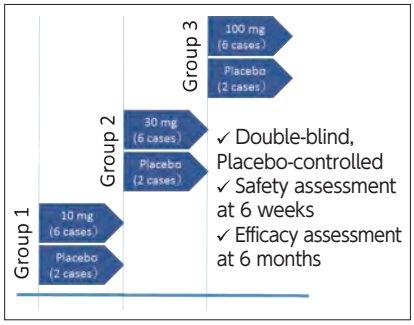
✓ Increase of regional blood flow

(Ishimaru et al. J Thorac Cardiovasc Surg 2013, Mizoguchi et al. AHA Scientific Sessions 2013 at Dallas)

Protocol of the clinical study



- ✓ Combined with CABG
- ✓ Placement over the LV
- ✓ Fibrin spray



- ✓ Double-blind, Placebo-controlled
- ✓ Safety assessment at 6 weeks
- ✓ Efficacy assessment at 6 months

【Inclusion criteria】
- ✓ Isolated CABG
- ✓ LVEF ≦ 40%
- ✓ More than 20 years of age

【Exclusion criteria】
- ✓ Irreversible liver/kidney damages
- ✓ Malignant tumour
- ✓ Diabetic
- ✓ Alcoholic/Drug abuse
- ✓ Psychiatric disorder
- ✓ Allergy for gelatin/aprotinin

Condition : Severe ischemic cardiomyopathy
Marketability : ¥3 billion/year (10,000 sufferers in Japan)
Patents : 5 patent applications submitted (corporate collaboration)
Technical features : Novel cell-free in vivo regenerative therapeutic agent

Inquiries
Department of Medical Innovation, Osaka University Hospital
2-2 Yamadaoka, Suita, Osaka 565-0871, Japan Tel : +81-6-6210-8289 Fax : +81-6-6210-8301
e-mail : dmi@dmi.med.osaka-u.ac.jp URL : http://www.dmi.med.osaka-u.ac.jp