

The jury is out..... Why ?

<u>Study</u>	<u>Effects</u>	<u>Design</u>	<u>Timing of Cell Tx</u>	<u>Cell Type</u>
BOOST 30/30	LVEF - controlled	randomized- controlled	4-8 days post PCI (gelatine sedimentation)	all nucleated BMCs
REPAIR-AMI 95/92	LVEF -	placebo- controlled	3-6 days post PCI	MN-BMCs only (Ficoll)
Janssens 32/34	LVEF ~	placebo- controlled	24 hours post PCI	MN-BMCs only Ficoll)
ASTAMI 47/50	LVEF ~	randomized- controlled	4-6 days post PCI	lymphocytic BMCs (Lymphoprep™)

Procedural issues such as timing of cell transfer and cell type may be critical and need to be further refined

Proposed Mechanism of Action of Cell Therapy

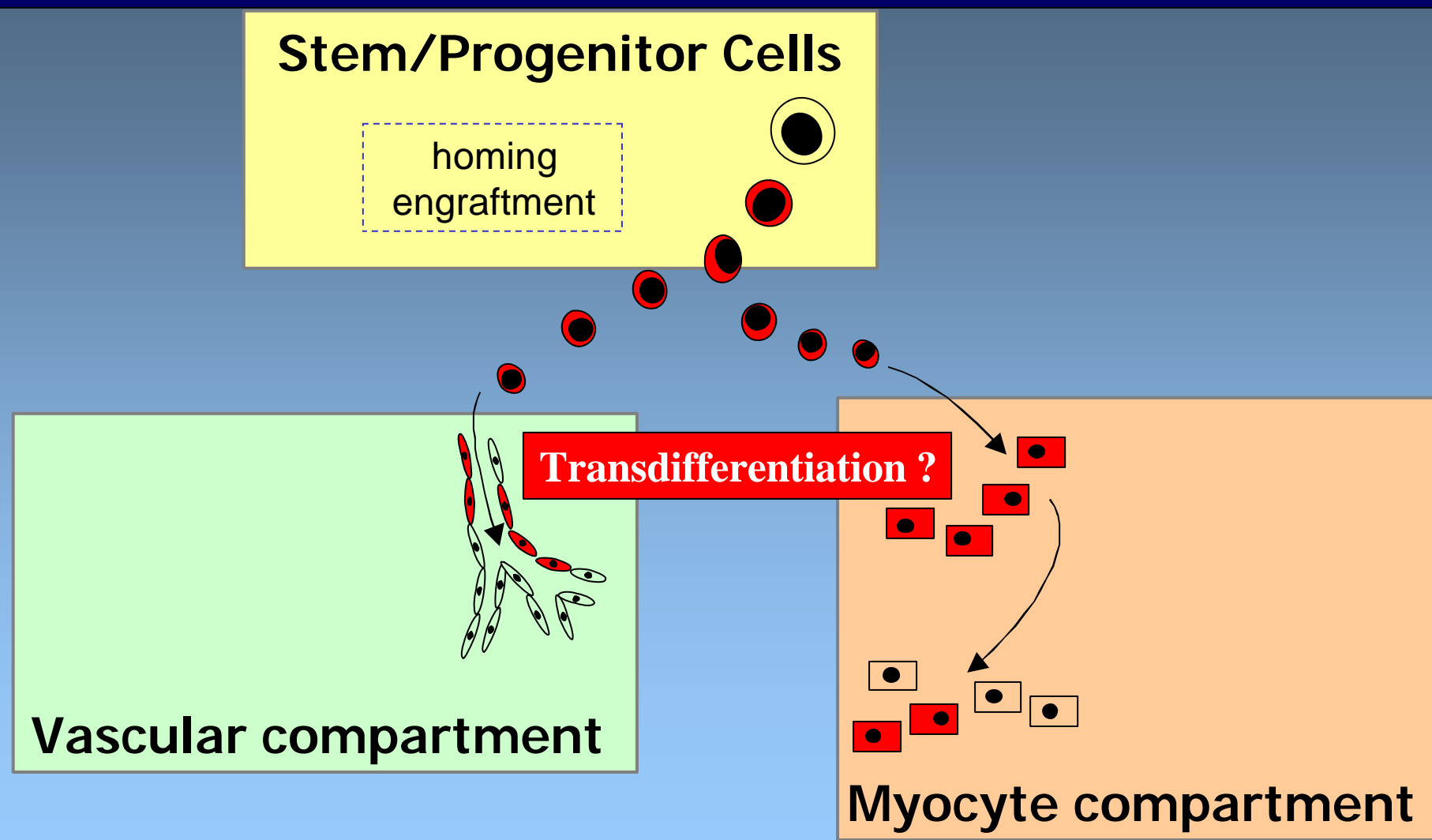
Stem/Progenitor Cells

homing
engraftment

Transdifferentiation ?

Vascular compartment

Myocyte compartment



Proposed Mechanism of Action of Cell Therapy

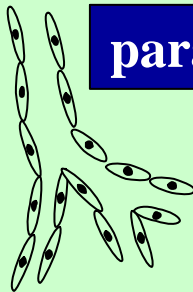
Stem/Progenitor Cells

homing
engraftment



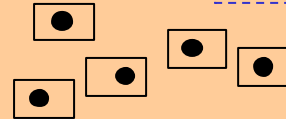
paracrine effects ?

apoptosis ↓
Proliferation
differentiation
SPC-recruitment



Vascular compartment

apoptosis ↓
hypertrophy
proliferation (?)
SPC-recruitment



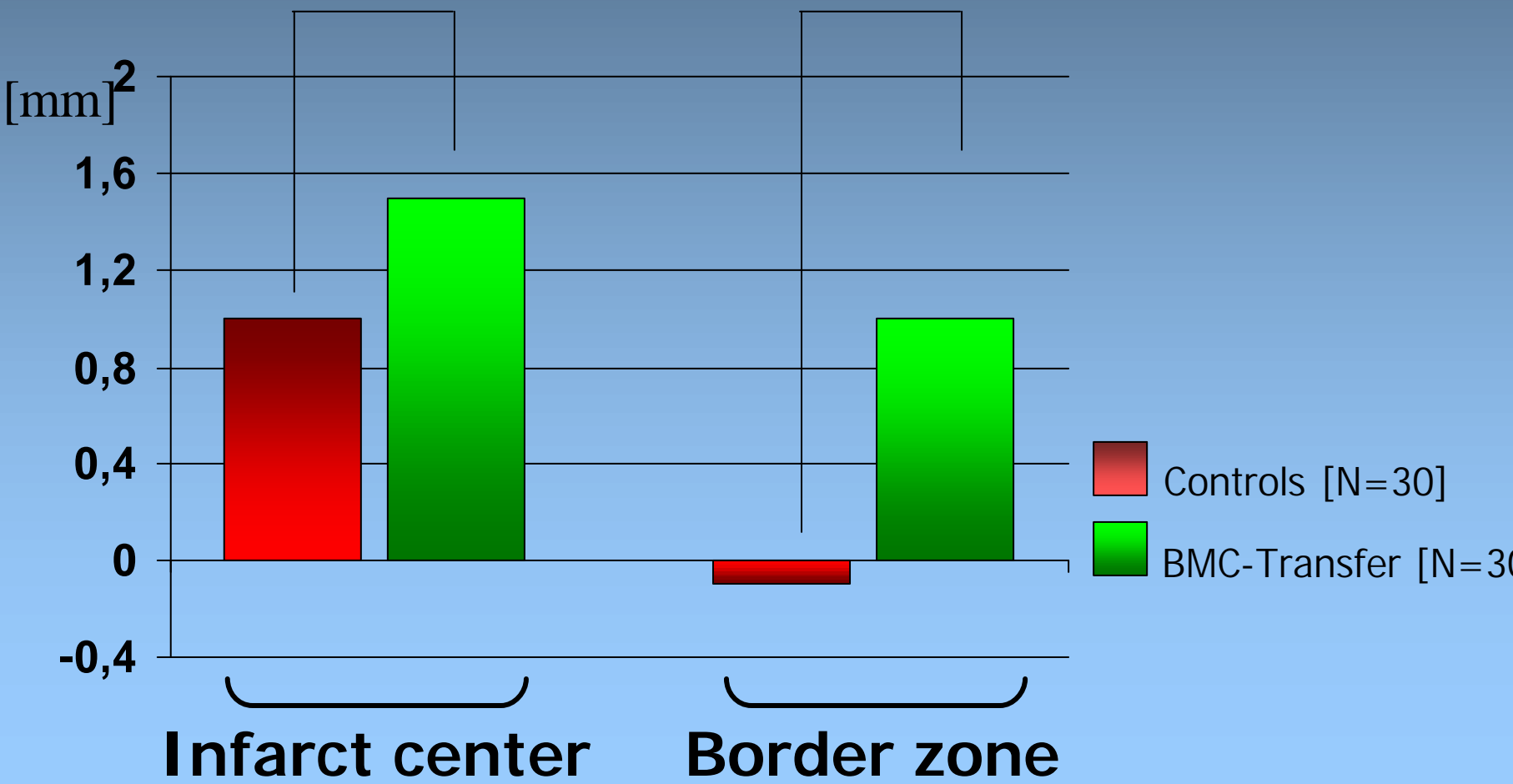
Myocyte compartment

Effects of BMC Therapy on Regional LV Function

Change baseline $\text{\textcircled{R}}$ 6 months

P = 0.32

P = 0.03



Experimental Studies of Cell Therapy post AMI

<i>Species</i>	<i>Cell population</i>	<i>Effects</i>
Mouse	Lin ⁻ /c-kit ⁺ cells	LV-function -
Rat	Ac-LDL ⁺ cells	capillary density ↑ fibrosis ↓
Rat	CD34 ⁺ cells	neoangiogenesis ↑ LV-function -
Rat	5AZA cells	LV perfusion ↑ LV function -
Rat	unselect. BM cells	LV function -
Pig	CD31 ⁺ cells	neoangiogenesis ↑
Pig	unselect. BM cells	collaterals ↑ LV function -

Tomita et al., *Circulation* (1999); Kobayashi et al., *J Surg Res* (2000); Orlic et al., *Nature* (2001); Fuchs et al., *JACC* (2001); Kamihata et al., *Circulation* (2001); Jackson et al., *J Clin Invest* (2001); Kocher et al., *Nat Med* (2001); Kamihata et al., *ATVB* (2002); Kawamoto et al., *Circulation* (2001, 2003)

Haematopoietic stem cells improve cardiac function and perfusion after infarction without permanent cardiac engraftment

