



# The JIKEI Heart Study

**The Largest Cardiovascular  
Intervention Trial in a Japanese  
population**



# Background

- **Drugs that inhibit the RAAS, such as the ARBs, have demonstrated clinical benefits in patients at risk for, or with existing, cardiovascular diseases**
- **Evidence of these benefits is largely lacking in Asian populations**





# The JIKEI HEART Study

- Investigator initiated and conducted
- Prospective, randomised, open-label, blinded endpoint (PROBE)
- 3081 Japanese patients with high blood pressure, coronary heart disease and/or heart failure
- Valsartan vs non-ARB-based therapy to achieve aggressive BP target of 130/80 mm Hg





# Study design

## ■ Study hypothesis:

- Valsartan will improve morbidity and mortality when added to conventional therapies in Japanese patients with hypertension and cardiovascular disease

## ■ Primary endpoint:

- Composite of CV mortality and morbidity
  - Stroke or TIA MI, hospitalisation for CHF or angina pectoris, dissecting aneurysm of the aorta , lower limb arterial obstruction, doubling of serum creatinine or transition to dialysis



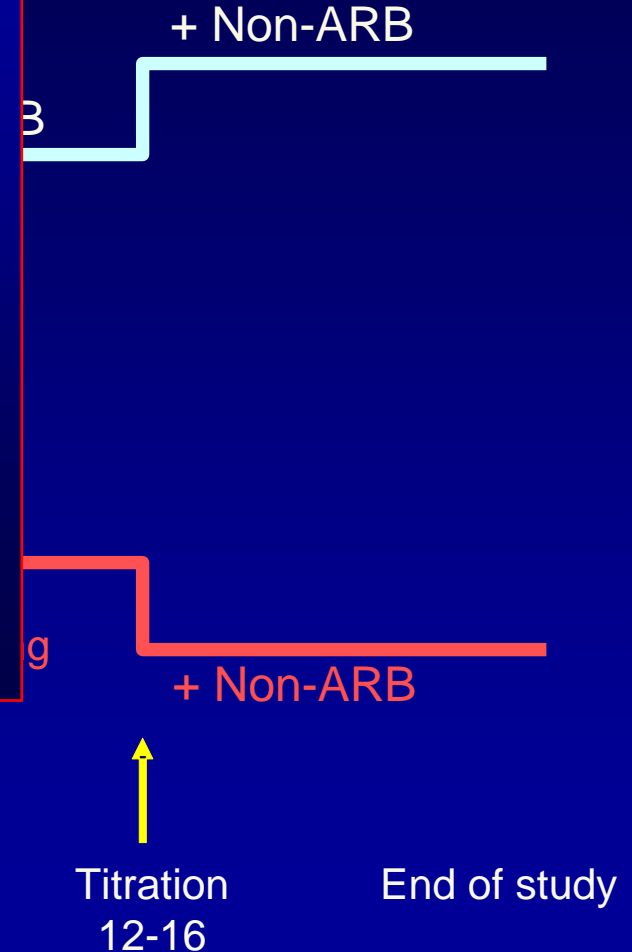


# Treatment schedule

## Medications at baseline

<u>Medication</u>	<u>Valsartan arm</u> (N=1,541)	<u>Non-ARB arm</u> (N=1,540)
CCB	1041 (68%)	1011 (66%)
ACE-I	548 (36%)	525 (34%)
β -blocker	486 (32%)	502 (33%)
α -blocker	74 (5%)	93 (6%)
Thiazide	29 (2%)	39 (3%)
Anti-aldosterone agent	52 (3%)	64 (4%)
Other diuretics	117 (8%)	126 (8%)
Statin	461 (30%)	490 (32%)
Fibrate	42 (3%)	37 (2%)

Data are means.



-4

Randomisation  
0

Titration  
8-12

Titration  
12-16

End of study

(Weeks)





# Baseline characteristics

	<u>Valsartan arm</u> (N=1,541)	<u>Non-ARB arm</u> (N=1,540)
<b><u>Clinical characteristics</u></b>		
Male	1,020 (66%)	1,023 (66%)
Female	521 (34%)	517 (34%)
Age (years)	65 (10)	65 (10)
Body-mass index (kg/cm <sup>2</sup> )	24 (3)	24 (3)
Current smoker	259 (17%)	262 (17%)
Systolic blood pressure (mmHg)	139.2 (11.4)	138.8 (10.6)
Diastolic blood pressure (mmHg)	81.4 (10.5)	81.4 (10.8)
Heart rate (beats/min)	71 (11)	71 (11)

Data are means.





# Baseline characteristics

<u>Medical history</u>	<u>Valsartan arm</u> (N=1,541)	<u>Non-ARB arm</u> (N=1,540)
Hypertension	1358 (88%)	1341 (87%)
Coronary heart disease	514 (33%)	522 (34%)
Heart failure	176 (11%)	174 (11%)
Hyperlipidaemia	812 (53%)	813 (53%)
Diabetes mellitus	315 (20%)	314 (20%)





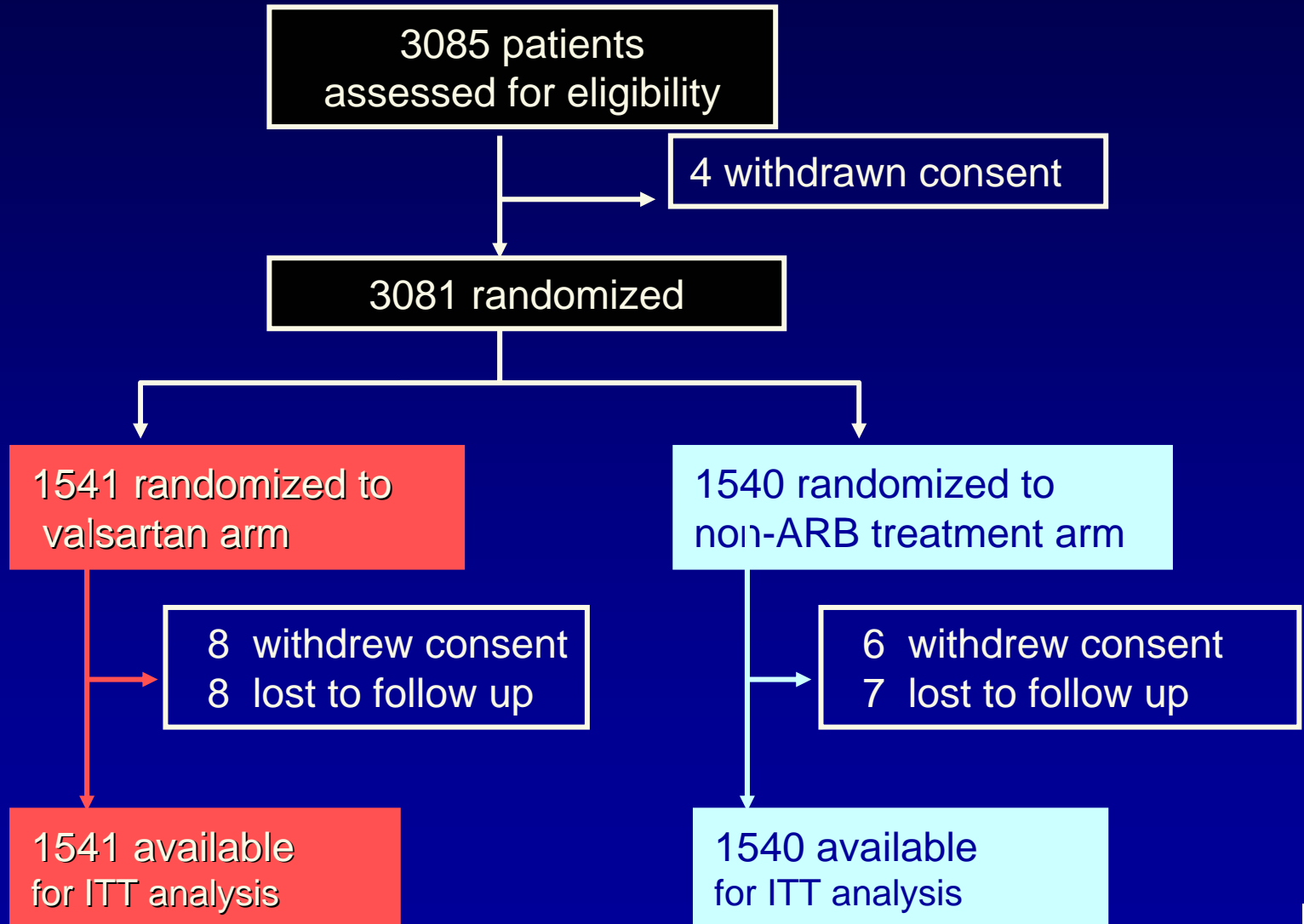
## Unequivocal benefit

**On a recommendation from the DSMB the study was halted early for ethical reasons, after just over 3 years, due to unequivocal benefit from valsartan**





# Trial profile





# Aggressive blood pressure control

<u>Trial</u>	<u>Journal</u>	<u>Baseline</u>	<u>Study end</u>
<b>HOT</b>	<i>Lancet</i> 1998	175 / 105	142 / 83
<b>CAPP</b>	<i>Lancet</i> 1999	161 / 99	150 / 90
<b>STOP-2</b>	<i>Lancet</i> 1999	194 / 98	159 / 81
<b>ALLHAT</b>	<i>JAMA</i> 2000	145 / 83	136 / 76
<b>NORDIL</b>	<i>Lancet</i> 2000	173 / 106	151 / 88
<b>INSIGHT</b>	<i>Lancet</i> 2000	173 / 99	138 / 82
<b>LIFE</b>	<i>Lancet</i> 2002	174 / 98	145 / 81
<b>VALUE</b>	<i>Lancet</i> 2004	154 / 88	138 / 79
<b>ASCOT-BPLA</b>	<i>Lancet</i> 2005	164 / 95	137 / 78
<b>JIKEI HEART</b>		139 / 81	131 / 77

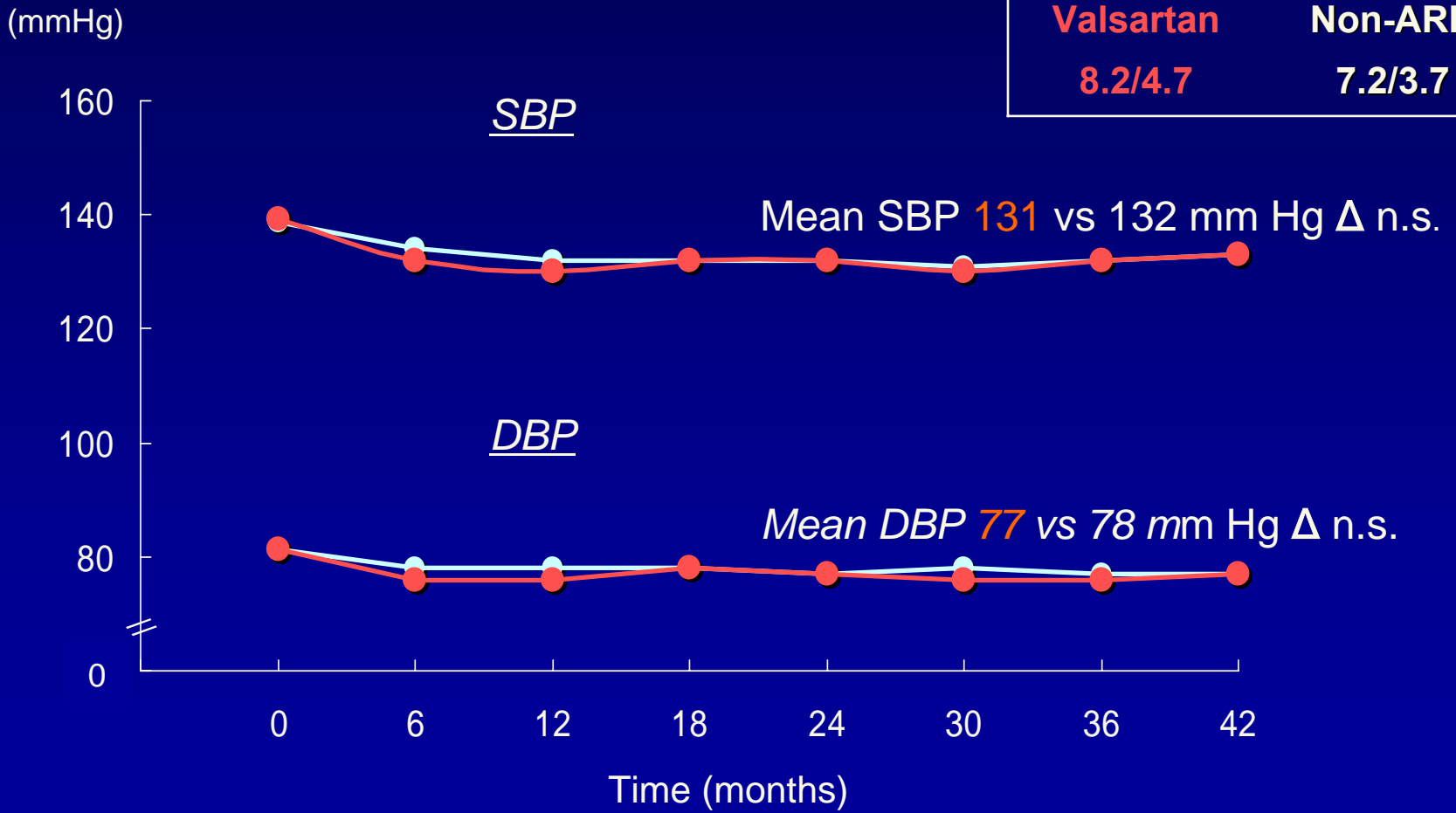




# Blood pressure results

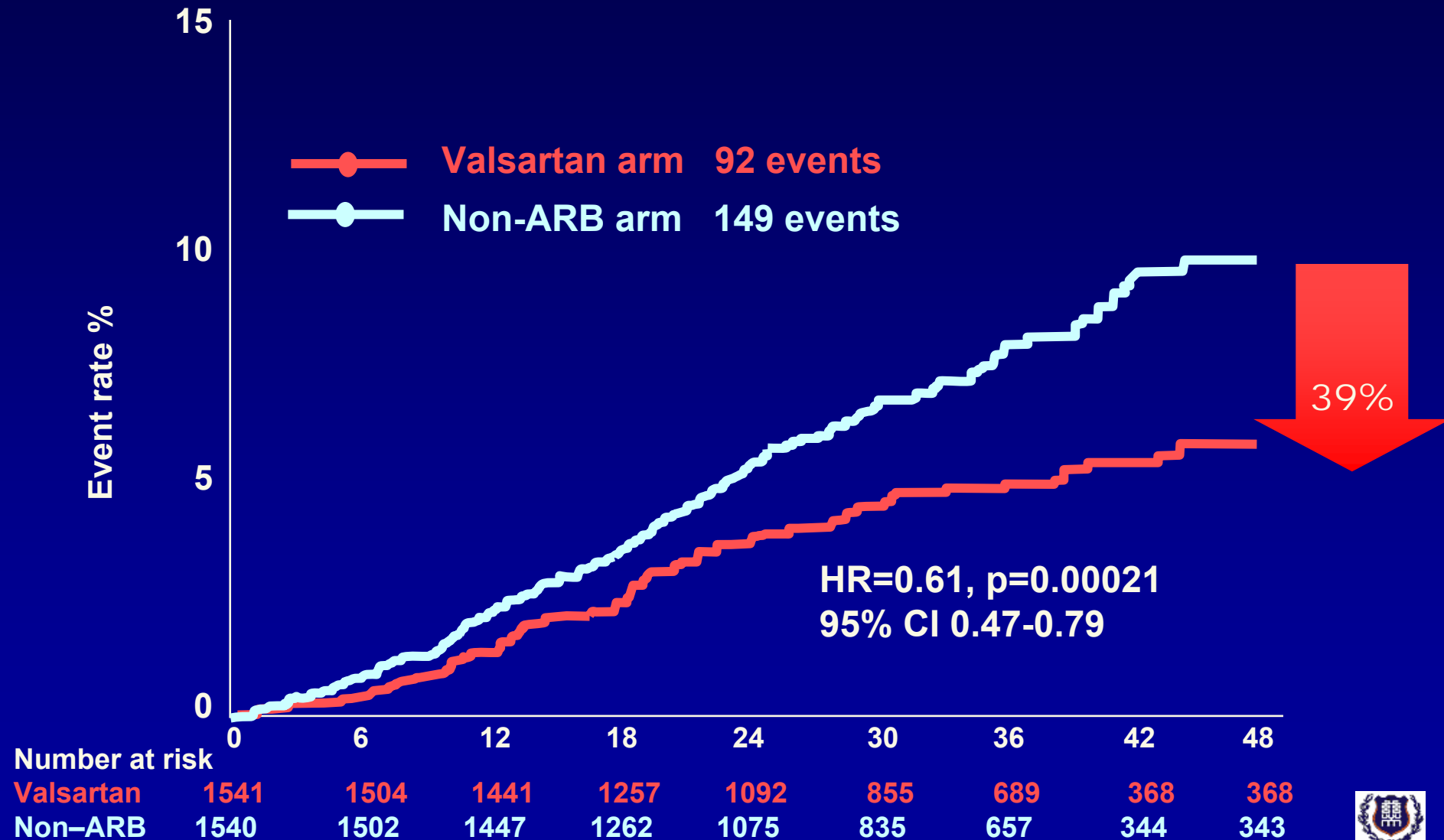
- Valsartan arm (N=1,541)
- Non-ARB arm (N=1,540)

Reductions from baseline	
Valsartan	Non-ARB
8.2/4.7	7.2/3.7



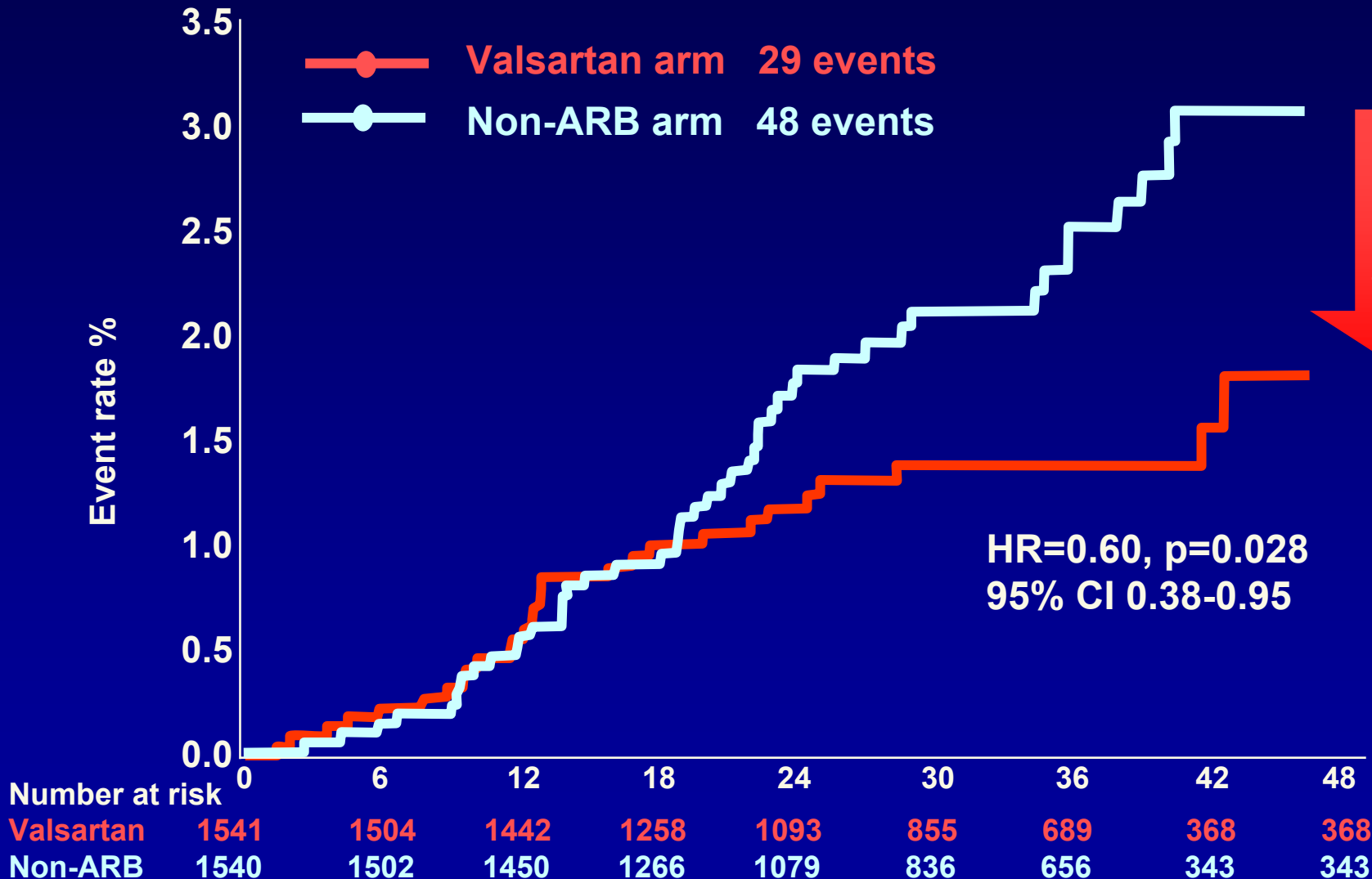


# Primary endpoint





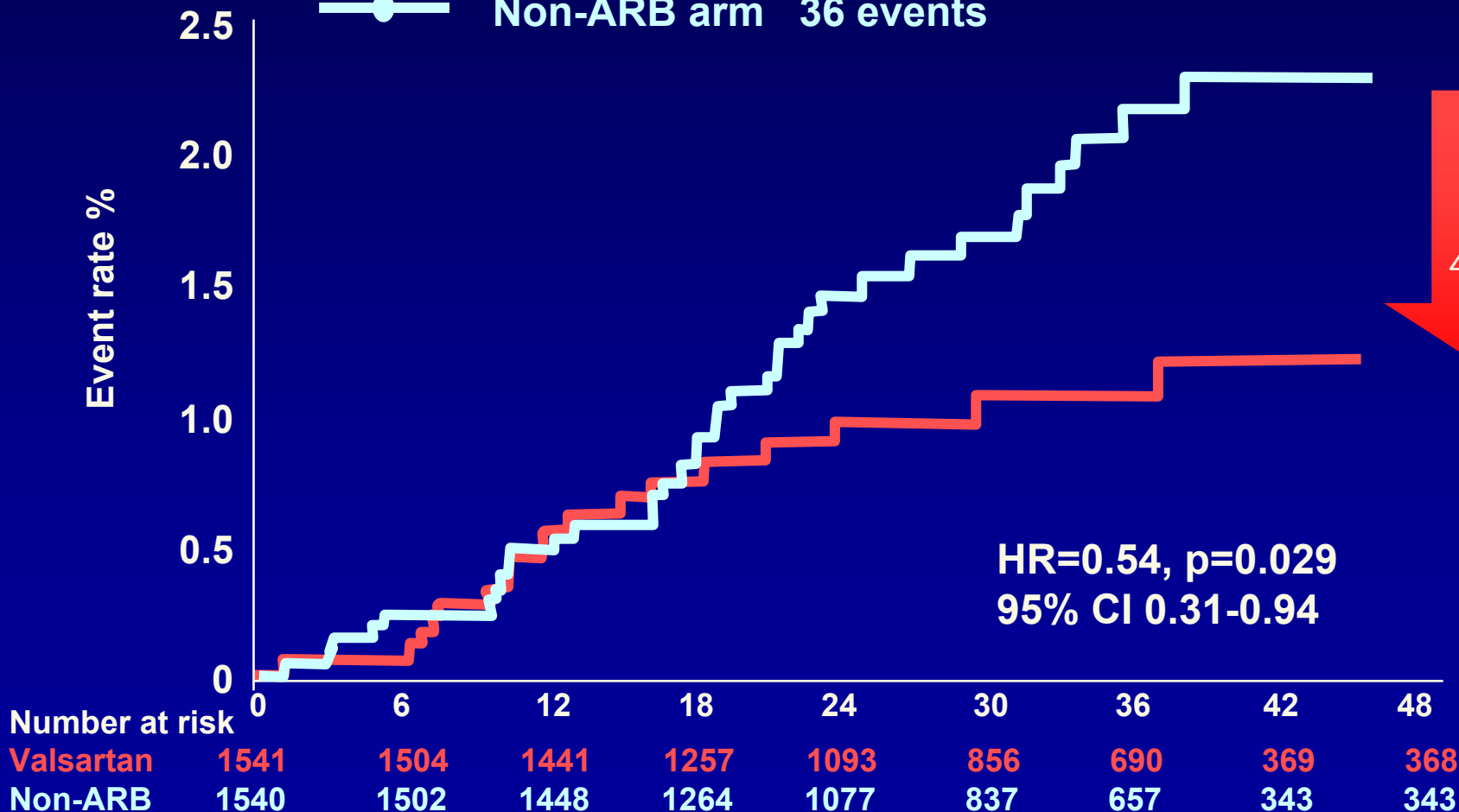
# New or recurrent stroke





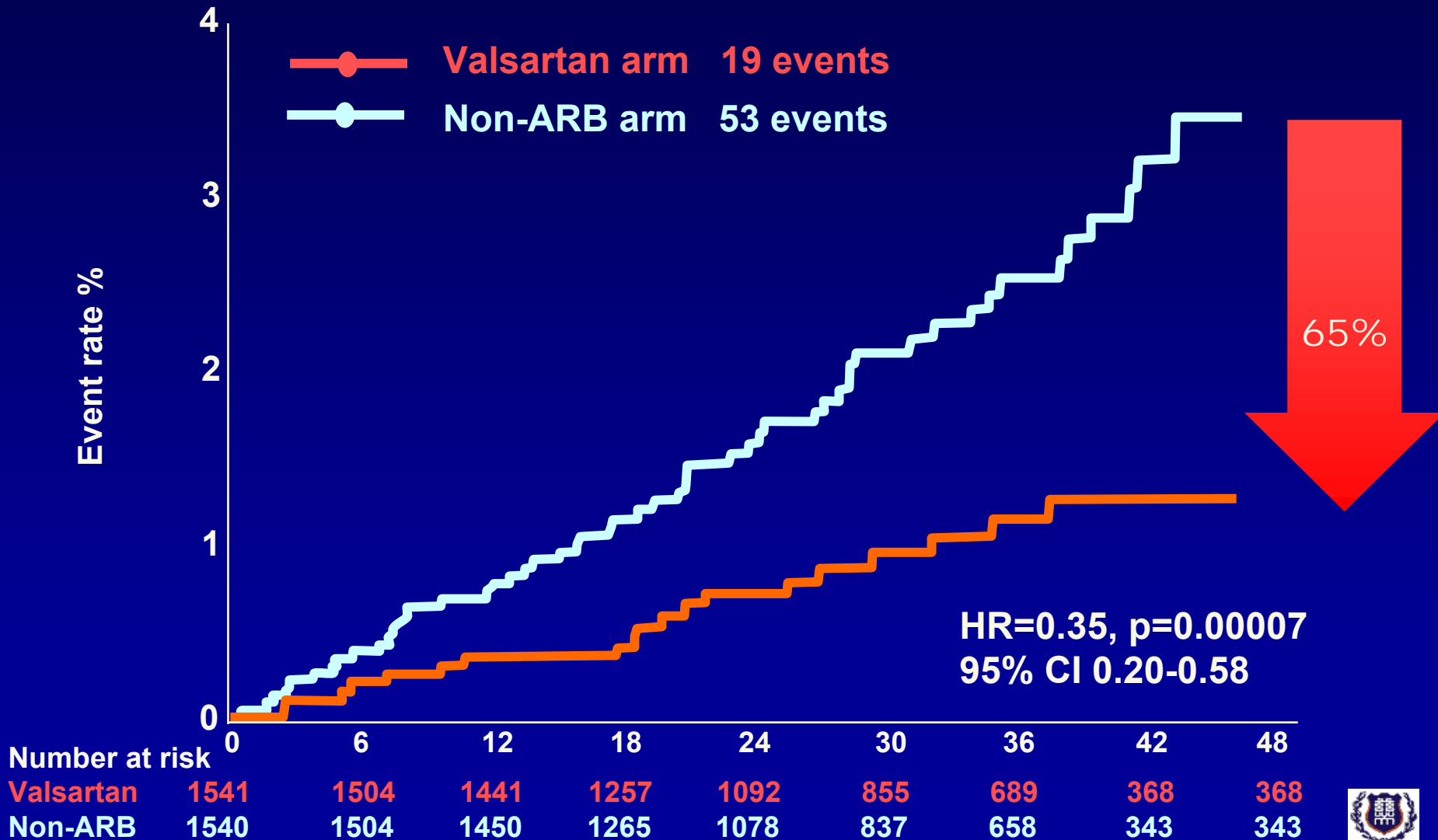
# Hospitalisation for heart failure

—●— Valsartan arm 19 events  
—●— Non-ARB arm 36 events



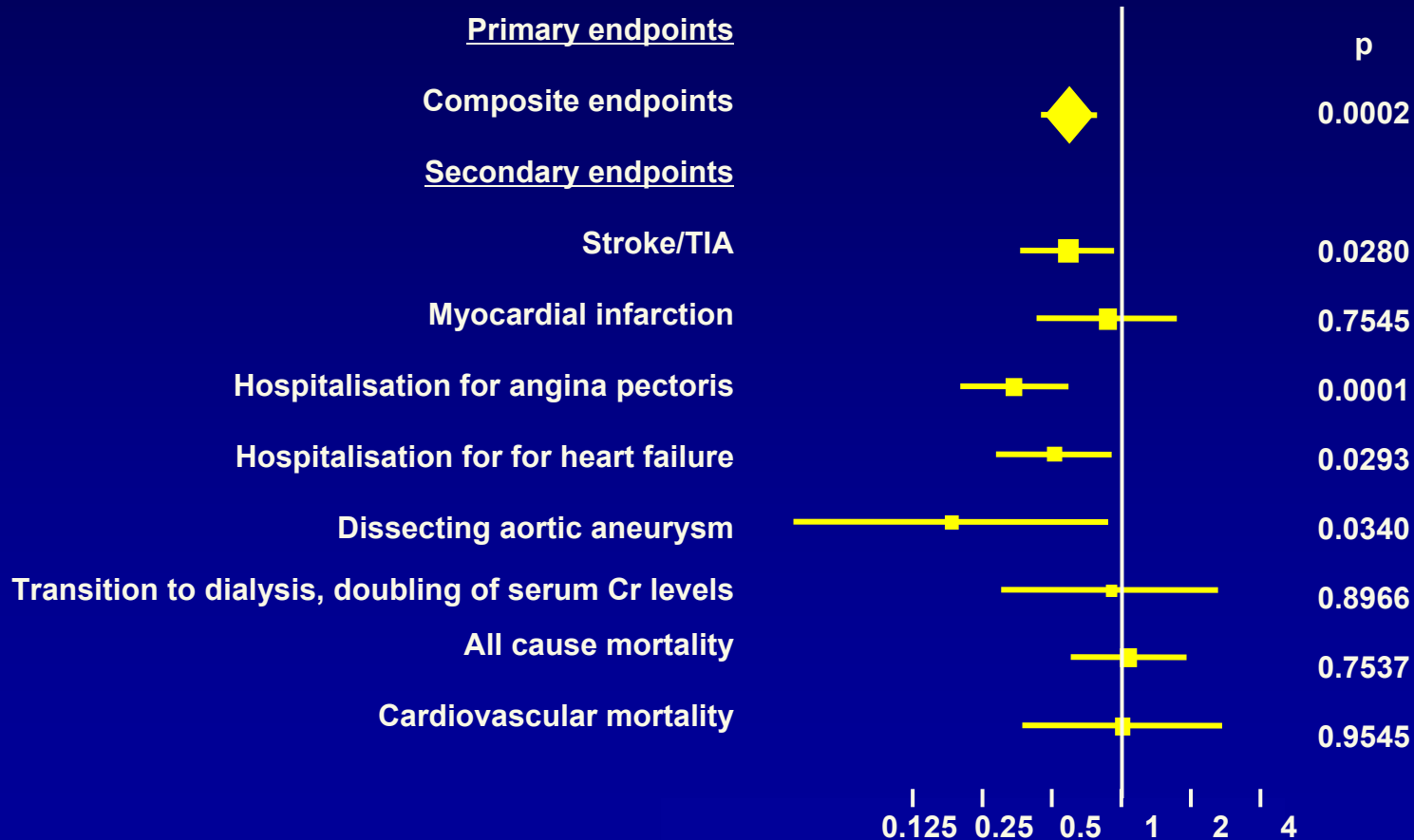


# Hospitalisation for angina pectoris





# Effect of treatment on endpoints





# Clinical relevance

- **For the first time, the clinical benefits of valsartan added to the benefits from blood pressure control, are extended to an Asian population**
- **The JIKEI Heart Study results are highly relevant to clinical practice**
- **We have to consider not only aggressive blood pressure control but also which blood pressure drug is the best choice to prevent outcomes**





# Study organisation

## Executive Committee

Seibu Mochizuki (Chair, The Jikei University School of Medicine)

Bjorn Dahlöf (Co-chair, Sahlgrenska University Hospital/Östra, Göteborg, Sweden).

## Steering Committee

Executive Committee + Mitsuyuki Shimizu, Ikuo Taniguchi, Katsunori Ikewaki, Kenichi Sugimoto, Kazuhiko Ogawa, Tsuneo Mizokami, Takahiro Shibata, Satoru Yoshida, Kenichi Hongo, Hideki Sasaki, Naofumi Aoyama, Hidenori Yagi, Takayuki Ogawa, Syunrou Minami, Fumiko Okazaki, Kiyoshi Kanae, Masayuki Taniguchi, Shingo Seki, Makoto Yoshikawa, Tatsuo Yamazaki, Taku Yamada, Mie Kawai, Hidetoshi Kajiwara, Kenji Noma (The Jikei University School of Medicine), Tatsuyuki Onodera (West-Saitama Central Hospital), Shinichiro Ishikawa, Yusaku Hayashi (Tsunan Metropolitan Hospital), Hidefumi Mikawa (Fuji City Central Hospital), Kenichi Maie, Nobunori Tominaga (Atsugi Metropolitan Hospital), Makoto Muto (Saitama Cardiovascular and Respiratory Centre), Noriaki Yoshitake, Hideaki Suzuki (Shonan Hospital), Osamu Aizawa (Oarai-kaigan Hospital), Kiyofumi Suzuki (Seki Hospital), Tetsushi Ito (Sakuragaoka General Hospital)





# Study organisation

## Endpoint Committee

Masatsugu Horiuchi (Chair, Ehime University)

Junichi Yamazaki (Toho University)

Hiromi Rakugi (Osaka University)

## Safety Committee

Shigeru Kageyama (Chair)

Tetsuo Sato, Masato Matsushima, Shigeto

Murakami, all from The Jikei University School of Medicine.





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