

Telmisartan Randomised Assessment Study in ACE-I Intolerant Patients with cardiovascular Disease

Medical media backgrounder

A first in cardiovascular protection

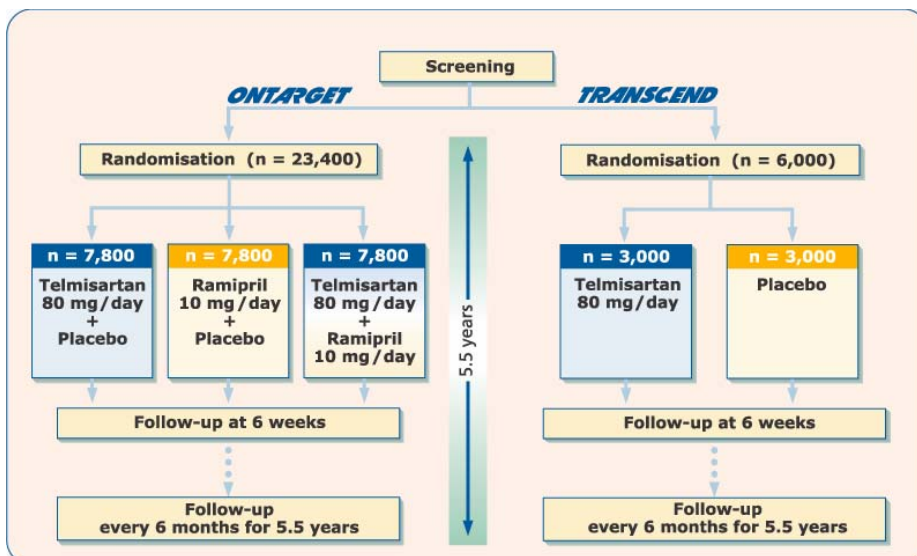
- ▶ TRANSCEND® is the first trial to examine the cardiovascular protective benefits of an ARB (MICARDIS® / telmisartan) compared with placebo in high-risk patients already receiving the best standard of care but who cannot tolerate ACE-inhibitors.

Improving care for high-risk patients

- ▶ Worldwide, nearly **1 in 4** people are intolerant to ACE-inhibitors.¹⁻³ Side effects associated with ACE-inhibitors include intolerable cough and angioneurotic oedema, which can lead to patients stopping their treatment, leaving them unprotected.¹⁻³
- ▶ TRANSCEND® is also the first cardiovascular trial to study a gender-balanced population, with 43% female participants.⁴
- ▶ The wide range of high-risk cardiovascular patients included in ONTARGET® reflects everyday clinical practice.

TRANSCEND Trial Design

- ▶ TRANSCEND® is a randomised, double-blind clinical trial which evaluated high-risk cardiovascular patients (n= 5,926) with normal or controlled blood pressure who were intolerant to ACE-inhibitors.⁴
- ▶ **Primary endpoint:** Cardiovascular death, heart attack, stroke and hospitalisation due to congestive heart failure.
- ▶ **Secondary endpoints:** Newly diagnosed heart failure, revascularisation, new-onset type 2 diabetes mellitus, nephropathy, cognitive decrease and dementia, and newly diagnosed atrial fibrillation.
- ▶ TRANSCEND® was not a hypertension study: patients with blood pressure >160/100 mmHg were excluded. Patients were included in the trial if they met the following criteria:⁴
 - ACE intolerant
 - Male or female aged 55 years or older
 - At high risk of developing a major cardiovascular event, with a history of:
 - Coronary artery disease
 - Peripheral arterial occlusive disease
 - Stroke or transient ischaemic attacks
 - Diabetes mellitus with end-organ disease.



The ONTARGET® Trial Programme is made up of both the TRANSCEND® and the ONTARGET® Trials

What do the results of The TRANSCEND® Trial show?

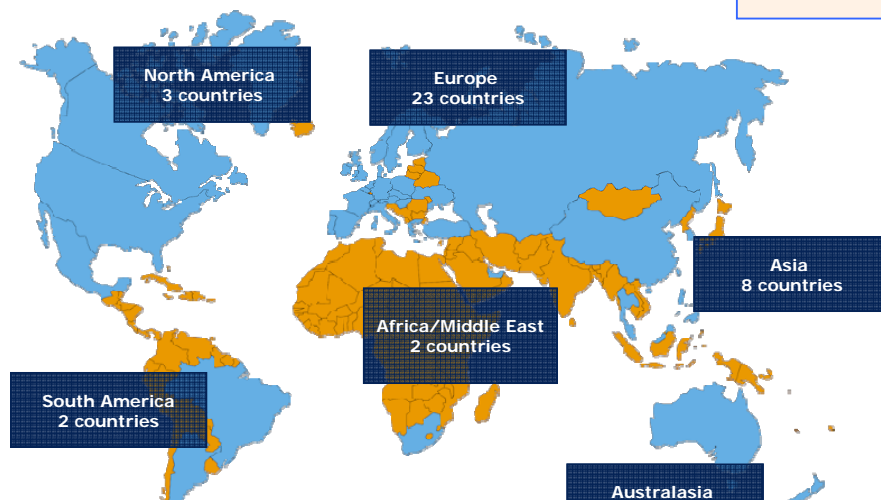
- ▶ MICARDIS® reduces the risk of cardiovascular death, heart attack and stroke in high-risk cardiovascular patients by 13% compared with those already receiving the current best standard of care ($p=0.048$)⁴, referring to the same endpoint as the primary endpoint of the landmark HOPE trial, published in 2000.⁵
- ▶ The pre-specified primary endpoint made up of the composite of cardiovascular death, heart attack, stroke and hospitalisation for congestive heart failure was non-significantly reduced by 8% ($p=0.223$)⁴
 - There was no impact on hospitalisation for congestive heart failure, which may be attributed to the high concomitant use of diuretics and beta-blockers in the placebo arm.⁴
 - All cardiovascular hospitalisations were, however, significantly reduced with MICARDIS® ($p=0.025$).⁴
- ▶ Therapy with telmisartan was well tolerated and was associated with a lower rate of discontinuation.⁴

What do the results of the ONTARGET®/TRANSCEND® Trial mean for physicians and patients?

- ▶ The ONTARGET® Trial has already demonstrated that MICARDIS® is as cardioprotective as, but better tolerated than, the ACE-inhibitor ramipril, the previous gold standard.⁶
- ▶ The TRANSCEND® Trial now shows that **ALL** hypertensive patients at high cardiovascular risk can now benefit from proven effective treatment with MICARDIS®, ensuring the best level of care.^{4,6}
- ▶ Being intolerant to ACE-inhibitors no longer means that patients may remain at risk of heart attack or stroke.^{4,6}
- ▶ MICARDIS® results in a significant reduction of all cardiovascular hospitalisations, which may have a positive pharmaco-economic impact on the cost and burden cardiovascular disease.

References:

1. Israili ZH, Hall WD. *Ann Intern Med* 1992 1; **117(3)**:234-42.
2. Matchar DB, et al. *Ann Intern Med* 2008; **148**:16-29.
3. Macaulay TE, Dunn SP. *US Pharmacist* 2007; **32 (2)**.
4. The TRANSCEND Investigators. *Lancet* Published online 31 August 2008.
5. The Heart Outcomes Prevention Evaluation Study Investigators. *N Engl J Med* 2000; **342**:145-53.
6. The ONTARGET Investigators. *N Eng J Med* 2008; **358**:1547-1559.



The ONTARGET® Trial Programme involved >31,000 patients and was conducted in over 700 centres across 40 countries⁶