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The CardioMetabolic ARB

ONTARGET® 

What is the ONTARGET® trial program?

- The ONTARGET® (ONgoing Telmisartan Alone and in combination with Ramipril Global Endpoint Trial) program is the largest, most ambitious ARB clinical study program ever undertaken and was designed to clarify whether telmisartan, marketed by Bayer HealthCare as Pritor®/Kinzalmono®, or ramipril, or a combination of the two, confers blood-pressure-independent cardio & vascular protection in high-risk patients whose blood pressure is well controlled. The trial was an academically-led study managed by the trials center at McMaster University, Hamilton, Canada.

ONTARGET® trial design

- ONTARGET® is a randomized, double-blind, double dummy clinical trial outcomes-led study. It investigated the role of the angiotensin II receptor blocker telmisartan in cardio and vascular protection.
- ONTARGET® included the broadest population ever in a study of this type: high-risk cardiovascular patients with a history of coronary heart disease, stroke, transient ischaemic attack, peripheral vascular disease or diabetes with target organ damage.
 - A high proportion of patients had previously received proven therapies:
 - Statins (61.6% at baseline, increasing to 70.6% by the end of the study)
 - Antiplatelet therapy (80.9% and 77.5% respectively)
 - Beta-blockers (56.9% and 56.9%) and
 - Diuretics (28.0% and 32.5%)
 - The wide range of high-risk cardiovascular patients included in ONTARGET® reflects everyday clinical practice.

The ONTARGET® trial investigated:

- Whether the ARB Pritor®/Kinzalmono® (telmisartan) 80mg is at least as effective as, and better tolerated than, the current gold standard ramipril 10mg (an angiotensin converting enzyme inhibitor, ACEI) in reducing the risk of CV-related events and death in high-risk CV patients
- Whether the combination of Pritor®/Kinzalmono® 80mg and ramipril 10mg (i.e. dual blockade of the renin-angiotensin-system, RAS) could provide a greater reduction in CV-related death and events than either treatment alone.



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The ONTARGET® secondary endpoints investigated:

- Newly diagnosed congestive heart failure
- Cardiovascular revascularisation procedure
- Newly diagnosed diabetes
- Cognitive decline/dementia
- New onset of atrial fibrillation

Results

Pritor®/Kinzalmono® – the only angiotensin II receptor blocker (ARB) shown to be as effective as ramipril²

- The results of ONTARGET® show that Pritor®/Kinzalmono® is as effective as the current gold standard ramipril in reducing the risk of cardiovascular death, heart attack, stroke and hospitalisation for congestive heart failure (combined primary endpoint) in high-risk CV patients already receiving optimal baseline care.²
- These events occurred in 16.66% of patients treated with Pritor®/Kinzalmono® and 16.46% of patients treated with ramipril.²
- The relative risk—the ratio of the probability of an event occurring in the telmisartan group versus the ramipril group—was 1.01, 95% CI 0.94-1.09.²

Pritor®/Kinzalmono® showed better tolerability

- The ONTARGET® results also show that Pritor®/Kinzalmono® is markedly better tolerated than ramipril 10mg in high-risk CV patients,² an important consideration as many patients are unable to tolerate treatment with ACEIs.³⁻⁵
- Increased tolerability also resulted in greater compliance with treatment – an essential factor for effective long-term treatment and protection against CV events.²
- The ONTARGET® trial also showed that combining ramipril and telmisartan (i.e. dual blockade of the renin-angiotensin system, RAS) provides no additional protective benefit for the overall patient population studied, answering an important question for the clinical community.²



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What do the results of the ONTARGET® trial mean for physicians and patients?

- Current treatment for hypertensive high-risk cardiovascular patients could be further improved by including Pritor®/Kinzalmono® in the treatment regimen.
- In addition to already proven powerful 24-hour blood pressure reductions, the ONTARGET® Trial has now proven that Pritor®/Kinzalmono® provides cardio and vascular protection for high-risk patients as effectively as ramipril and it is also better tolerated and associated with a better compliance.²
- The ONTARGET® trial program provides further evidence for the benefits of Pritor®/Kinzalmono® beyond those of blood pressure lowering alone.² Previously, the AMADEO trial showed that Pritor®/Kinzalmono® has the potential to provide renal protection as demonstrated by a significantly greater reduction in proteinuria compared to the ARB losartan.⁶

What is cardio & vascular protection?

- Cardio and vascular protection means protection of the vascular system, the heart and other target organs against damage which can cause a cardiovascular event including myocardial infarction (MI), stroke, congestive heart failure (CHF) and renal failure. Providing cardio and vascular protection is an important aim of patient management in cardiovascular disease. Providing cardio and vascular protection benefits patients by reducing cardiovascular morbidity and mortality as a result of preventing cardiovascular events.
- Cardiovascular disease (CVD) is the term given to a wide range of disorders affecting the heart and blood vessels including coronary heart disease (CHD), cerebrovascular disease, hypertension (high blood pressure) and peripheral vascular disease (PVD).
- Pritor®/Kinzalmono® provides powerful and consistent blood pressure reductions over a full 24-hour period,⁷⁻¹¹ particularly in the risky early morning hours when blood pressure surges^{11,12} and the risk of cardiovascular events is at its highest.^{12,13}
- The ONTARGET® trial has also proven that in addition to providing effective 24-hour blood pressure control, Pritor® /Kinzalmono® also provides cardio and vascular protection for high-risk cardiovascular patients, which has led to the to improved clinical outcomes in these patients.²



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Unique properties of Pritor®/Kinzalmono®

- The benefits of Pritor®/Kinzalmono® seen in the ONTARGET® trial could be attributed to the specific molecular structure that is demonstrably different from other ARBs and leads to pharmacological properties that make it unique amongst ARBs:
 - Insurmountable blockade of AT1-receptor
 - Slow rate of dissociation from the receptor
 - Highest volume of distribution of ARBs
 - Longest half-life of ARBs: effect maintained over 24 hours with single dose
 - High lipophilicity
 - High level of tissue penetration
 - Unique selective PPAR- γ modulations (SPPARM) that translate into a favourable glycaemic and lipid metabolism effect
- Pritor®/Kinzalmono® has been shown to achieve superior blood pressure lowering to losartan and valsartan.^{17,18} It has also been shown to achieve blood pressure lowering at least as effectively as enalapril, lisinopril, ramipril, amlodipine and atenolol, leading medicines in other classes.¹⁹⁻²³

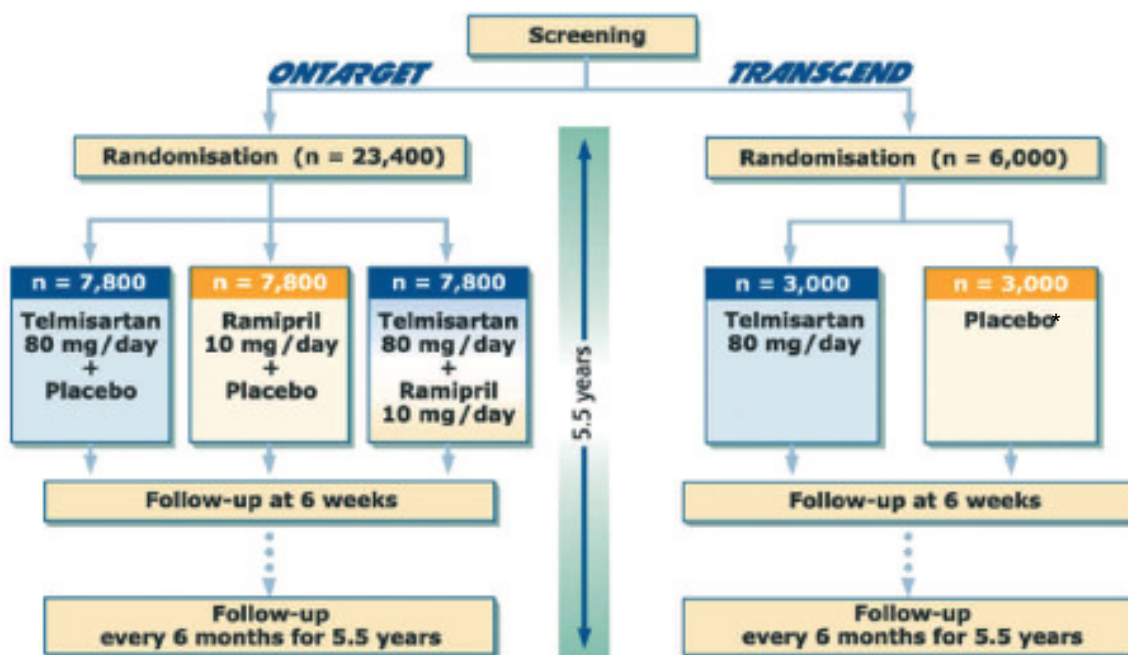


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TRANSCEND – a first trial in cardio & vascular protection

- TRANSCEND is the first trial to test the cardiovascular protective effect of Pritor®/Kinzalmono® compared with placebo on top of standard therapy (including antihypertensives, anti-platelets and statins) in individuals who are intolerant to ACE inhibitors. The first results from TRANSCEND are expected later in 2008.¹



* Best practise therapy, including statins, antiplatelet therapy, betablockers and/or other antihypertensives



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Medical Media backgrounder on the ONTARGET® Trial Programme - published in March 2008 – www.boehringer-ingenelheim.com 3