

# Amlodipine/valsartan single pill combination therapy in Chinese patients not controlled on previous monotherapy

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The majority of hypertensive patients requires combination therapy to reach target blood pressure (BP), usually a value <140/90 mmHg (1,2). On the basis of data available from published hypertension treatment trials, a rule of thumb has recently been proposed whereby approximately a third or less of unselected hypertensive patients will have their BP controlled with a single agent while two third need at least two drugs (3).

Hypertension is a chronic condition that requires long-term, in many instances lifelong treatment. One of the biggest problems in any chronic treatment, however, is the patients' adherence with drug therapy. Non-adherence is a complex and multifactorial phenomenon. Ample evidence points to the fact, that the therapy itself may be a major modulator of adherence, with drug class and thus tolerability, medication time-points (once, twice or three times daily) and especially the number of pills to be taken by the patient on a given day, the so-called pill-burden, being involved (4). It may therefore be suggested that any chronic therapy should be set up as simple as possible to improve the likelihood of adherence with the prescribed medication. Consequently, most of the recent hypertension guidelines recommend the use of fixed-dose (single-pill) combinations (SPC) when multiple drug therapy is indicated (1,2).

In the recent hypertension guidelines published by the American (ASH) and International Societies of Hypertension (ISH), which were endorsed by the Asia Pacific Society of Hypertension (APSH), only two antihypertensive dual combination treatments were recommended, renin angiotensin system (RAS) blockers plus either diuretic or calcium channel blockers (CCB) (2). In the British hypertension guidelines from 2011, recommendations are similar but preference is given to combining a RAS blocker

with a CCB (5). This illustrates the clinical relevance of single pill combinations containing either an ACE-inhibitor or an angiotensin receptor blocker (ARB) plus a CCB. One of the most extensively studied of such combinations is the ARB valsartan plus the CCB amlodipine which has been available as a SPC in many countries since 2009. The efficacy and safety of that combination have been demonstrated in several randomized controlled trials.

However, while blinded randomized trials remain the gold standard to demonstrate efficacy of any treatment, several shortcomings must also be acknowledged. One of these is the problem of patient selection in a clinical trial which may not resemble patient characteristics in a given region or clinical setting. It is therefore important to also investigate therapeutic strategies in prospective, open label, post-marketing observational studies.

Such a study on a SPC containing valsartan (160 mg) and amlodipine (5 mg) has recently been published by Hu *et al.* (6). The study population included 11,422 Chinese adults with essential hypertension from 238 sites and 29 provinces whose BP was not adequately controlled by previous monotherapy. After 8 weeks treatment with the dual combination mean BP had decreased by 27.1/15.2 mmHg ( $P<0.0001$ ). However, at the end of week 4, 6.1% of the patients with uncontrolled BP had been given additional antihypertensive agents, mostly diuretics. It is therefore important to note that after 4 weeks of treatment with the dual combination (before additional antihypertensives were given) BP was already decreased by a mean of 20.1/10.6 mmHg ( $P<0.0001$ ). Most importantly, patients were not "washed out" from their previous monotherapy but were directly switched to the valsartan/amlodipine SPC. Therefore, the observed effects resemble an additional decrease in BP on top of the effect of the previous

monotherapy.

These results are in good agreement with the outcome of a controlled prospective study which was also performed in patients whose BP was not normalized on antihypertensive monotherapy (7). Similar to the present study, 440 of these patients were also switched to valsartan 160 mg/amlodipine 5 mg SPC treatment. After 8 weeks of therapy without additional antihypertensives the fall in BP in that study averaged 16.5/9.3 mmHg (7). Similar to the results obtained by Hu *et al.* there was no dependence of the BP lowering efficacy of the dual combination on the class of antihypertensives that was used before SPC treatment with valsartan/amlodipine was established.

The findings from this large observational study confirm the effectiveness of a dual combination containing valsartan and amlodipine given as a SPC in Chinese hypertensive patients.

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