GMRx2: single pill combination of telmisartan, amlodipine and indapamide to treat hypertension, including initial treatment

Two pivotal trials of novel low dose triple combination

Funding: George Medicines Pty Ltd

Declaration of Interest: institutional (George Institute for Global Health and George Medicines); seconded to George Medicines, no personal financial interest

Professor Anthony Rodgers on behalf of the GMRx2 Investigators

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Declaration of interest

- I have nothing to declare

Phase III trials demonstrate potential of novel low-dose triple combination pill to transform management of hypertension

Globally, over a billion adults have hypertension and control rates remain suboptimal in all countries, principally due to continued use of low-efficacy regimens such as monotherapy

GMRx2 was developed to deliver synergistic efficacy benefits of triple therapy, while maintaining tolerability, in a single pill expected to improve patient adherence

Multi-mechanism combination of 3 existing best-in-class medicines in novel low- and ultra-low dose pills

All safety and efficacy endpoints met in both trials–

- Significantly reduced blood pressure and improved control rates vs dual therapy or placebo
- Good tolerability and no increase in adverse event withdrawals

Combination pill offers potential new therapeutic option for initial/ early treatment and in later steps of therapy

Conclusion

Novel low-dose triple combination achieved all efficacy endpoints in two phase III pivotal trials

Good tolerability with no difference in primary safety outcome

Potential new therapeutic option:

- Existing use in later steps of therapy
- Novel use for initial/early treatment

Help address unmet need to improve control of blood pressure using effective, simple, tolerable combinations.

Methods

Phase III program in Australia, Czech Republic, New Zealand, Poland, Sri Lanka, United Kingdom and the USA

Placebo-controlled trial

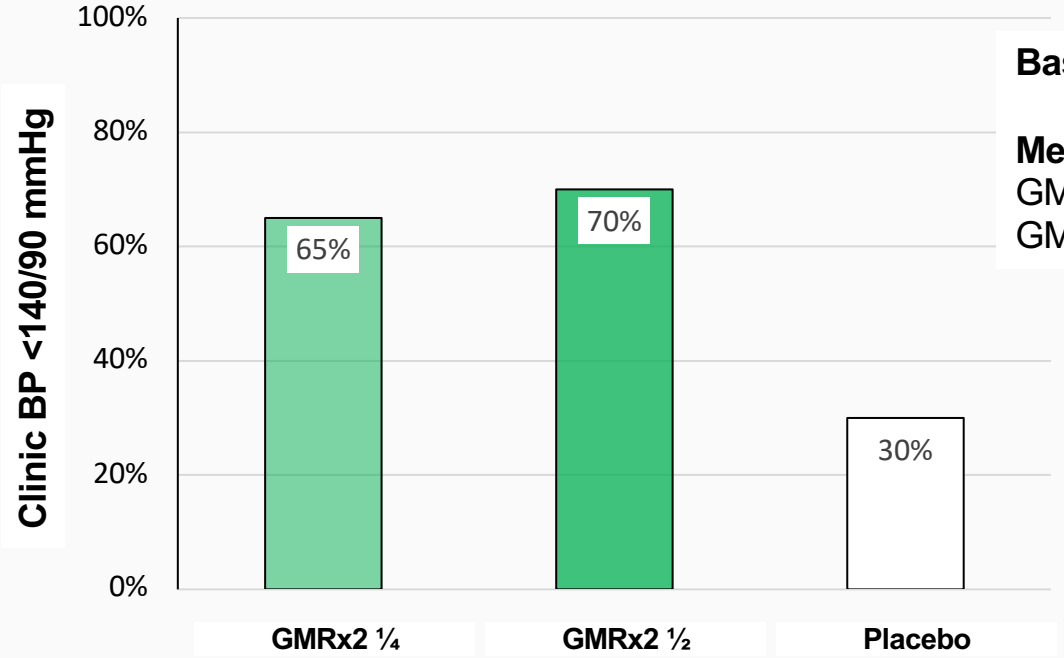
- GMRx2 (ultra-low and low-dose) vs placebo
- N=295
- Tested ‘full’ efficacy and tolerability

Active-controlled trial

- GMRx2 (low-dose and standard dose) vs 3x dual combinations
- N=1395
- Tested contribution of each component to efficacy and tolerability

Program designed to secure regulatory approval in the USA

Placebo-controlled trial – key efficacy results



Baseline home BP:139/86 mmHg

Mean home BP reductions
GMRx2 ¼: 7.3/4.0 mmHg
GMRx2 ½: 8.2/5.5 mmHg

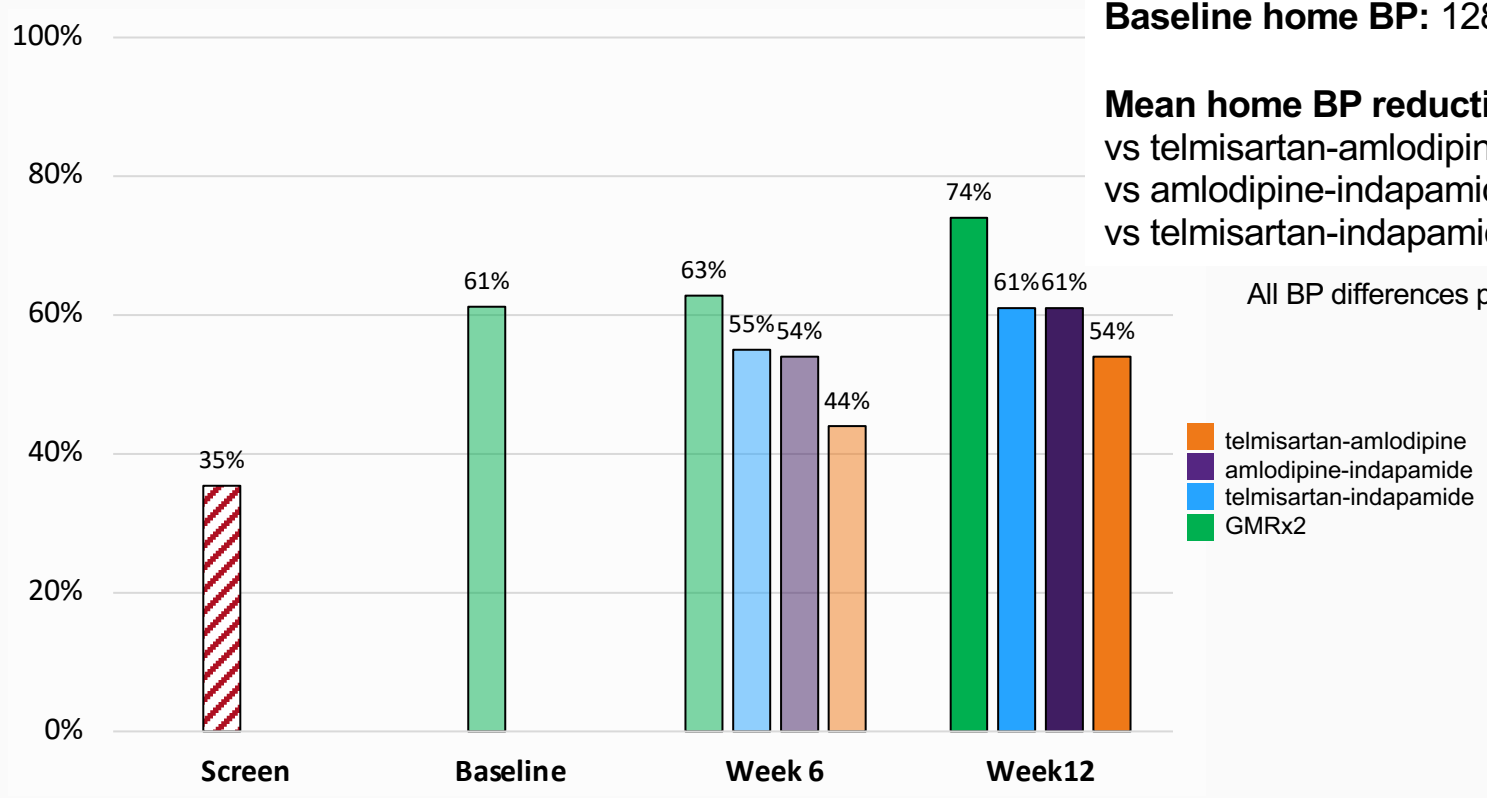
All BP differences p<0.0001

Active-controlled trial – key efficacy results

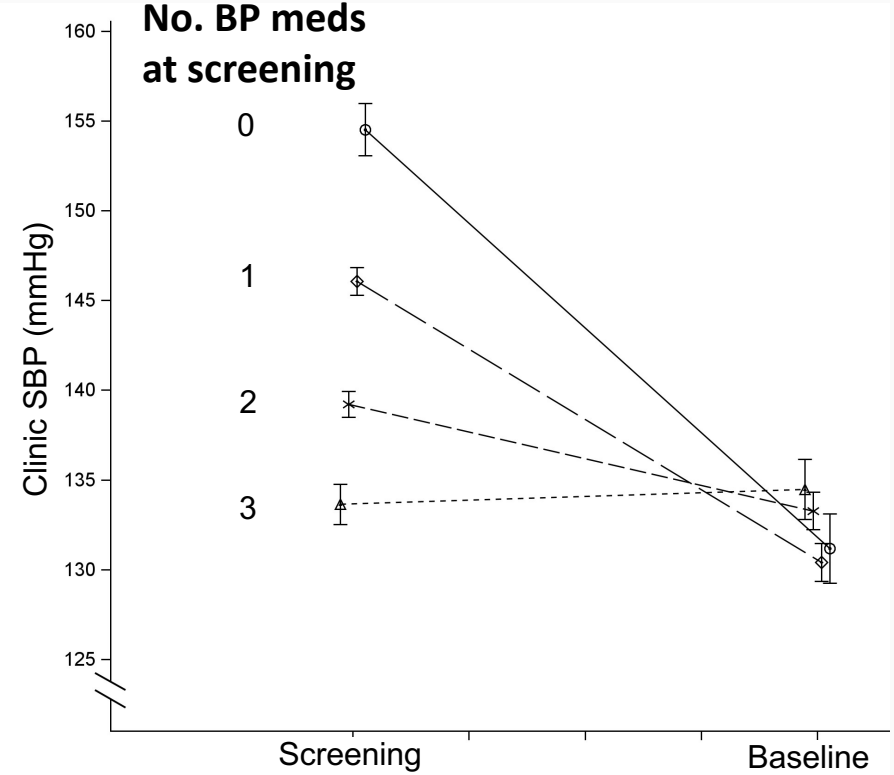
Baseline home BP: 128/78 mmHg

Mean home BP reductions (mmHg)
vs telmisartan-amlodipine: 5.4/3.4
vs amlodipine-indapamide: 4.4/3.6
vs telmisartan-indapamide: 2.5/2.1

All BP differences p<0.0001



BP during 4 week active run-in when participants were switched from 0-3 BP meds to GMRx2 ½



Tolerability results

No significant differences in any of the primary safety outcome comparisons of treatment-withdrawal

No increases in Serious Adverse Events

Expected increases in non-serious events:

Symptoms of hypotension

- **active trial: 6% GMRx2 vs 1-4% duals**
- **placebo trial: 4-5% GMRx2 vs 0% placebo**

Also expected increases in low potassium levels

Summary: Novel low-dose triple combination achieves all efficacy outcomes: demonstrates potential to transform hypertension management

Potential new therapeutic option for hypertension, including initial treatment

Offers the potential of increased efficacy and good tolerability

Important advance for management of high blood pressure, our leading cause of stroke, heart disease and other cardiovascular diseases

“The clinical and public health significance of these findings is considerable, given the continuing global disease burden of hypertension.

“Control rates are suboptimal in all countries, even where access and affordability are not major factors, principally due to continued use of low-efficacy regimens.

“With evidence increasingly showing the value of lower blood pressure targets, the potential of an effective, low-dose, triple combination with a good safety profile for the early treatment of hypertension should not be underestimated.”

Professor Anthony Rodgers, Chief Medical Officer of George Medicines and Professorial Fellow at The George Institute for Global Health