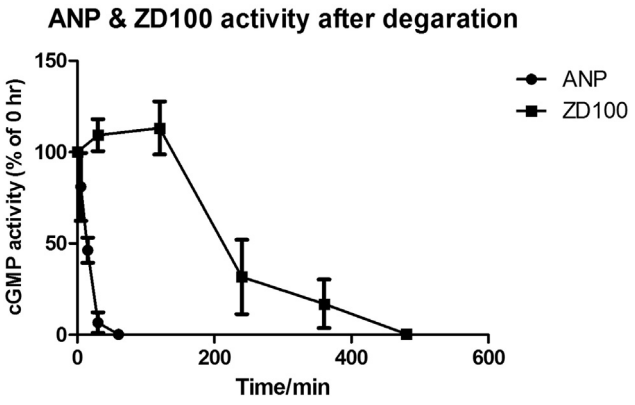

Figure 1.

Conclusion: We conclude that ZD100 retains the activity to stimulate cGMP production through pGC-A as ANP and is much more resistant to NEP degradation. These in vitro mechanistic studies support ZD100 as a potent novel natriuretic and diuretic agent for the treatment of HTN and resistant HTN.

Keywords: Resistant hypertension; ZD100; Neprilysin degradation

P-10

A first-in-human trial of a novel designer natriuretic peptide ZD100 in human hypertension

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Background: An unmet need is novel therapeutic agents for resistant hypertension (RH) which has no FDA approved drugs or devices. ZD100 is a novel particulate-guanylyl-cyclase A (GC-A) receptor activator designed at the Mayo Clinic which goes beyond ANP in promoting natriuresis, inhibiting aldosterone and reducing blood pressure (BP) with greater activation of cGMP. Here we report findings in a Phase 1, a two part first-in-human (FIH), single ascending dose (SAD) and multiple ascending dose (MAD) trial which defined safety, maximum tolerated dose (MTD) with subcutaneous (SQ) administration of ZD100 to hypertensive subjects.
Methods: Part A was an open label sequential SAD design study with 3 cohorts of 4 stable hypertensive subjects each with systolic BP (SBP) greater than 140 mm Hg and diastolic BP (DBP) greater than 90 mmHg while on at least one standard-of-care anti-hypertensive. Each subject received a single SQ injection of ZD100. All subjects stopped all anti-hypertensive agents for 14 days prior to the study. Part B was a randomized, double-blind, placebo-controlled MAD design in 3 cohorts of 5 hypertensive subjects each on at least 3 medications at including a diuretic and angiotensin-converting enzyme inhibitor (ACEI) or angiotensin receptor blocker (ARB) and with BP $>$ 145/70 mmHg. SQ ZD 100 was administered once daily for three days The MTD was defined as a decrease in systolic BP of $\geq$ 30 mmHg. In Part B all subjects continued their anti-hypertensive medications.
Results: Part A: 3 cohorts were dosed at 1, 2.5 and 5μg/Kg respectively. The MTD was 5μg/Kg. BP was reduced with all doses. The maximal SBP and DBP reductions were -20 $\pm$ 18 mmHg and -12 $\pm$ 5 mmHg respectively which occurred in the 5ug/kg cohort. Both SBP and DBP were lower than baseline at 24 hours. Part B has been completed and the BP, pharmacokinetic and neurohumoral data are pending. ZD100 was well tolerated with no serious adverse events (SAE).
Conclusions: ZD100 in this first-in-human study was safe and highly effective in lowering systolic and diastolic BP with duration of 24 hours. These studies support further investigations in human RH with this novel designer peptide that activates the GC-A receptor and cGMP system.
Keywords: hypertension; natriuretic peptide

BLOOD PRESSURE MEASUREMENT/MONITORING

P-11

Prevalence of optimal blood pressure values in digital-savvy hypertensives

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Background: The recent SPRINT trial demonstrated the potential benefits of intensive management of systolic blood pressure to $<$ 120 mmHg.
Aim: To determine the prevalence of optimal systolic BP values in participants to a real-life digital-only BP registry and assessment service.
Population and Methods: 3250 consecutive subjects (74% males; 51$\pm$12 years old) that, unsolicited, joined a real-time BP -recording, -interpretation and -trend evaluation service (via smartphone-Health App and website platforms). Thru the digital platforms, each BP value, after consistency-checks, feeds a proprietary CE medical device certified algorithm providing both individual BP value interpretation and BP trend assessment. These latter are fed back to users on their smartphone and computer screens instantly. The service complies with the most strict data privacy, safety and security requirements.
Results: We collected 42316 BP measurements, overall. Systolic BP values were $<$ 120mmHg in 33% of instances, diastolic BP values were $<$ 80mmHg in 52% of instances, whilst both systolic and diastolic BP values were $<$ 120/80mmHg, respectively, in only 27% of instances. Conversely, according to the most commonly used normal thresholds of BP $<$130/85mmHg, 63% of systolic BP values were ''normal'', 68% of diastolic BP values, and 52% of both systolic and diastolic BP values.
Conclusion: In population of digital-savvy subjects, who are so aware of the need of controlling their BP so that they subscribed a digital BP evaluation service, the largest majority (63%) of BP measurements does not reach the optimal ($<$120/80mmHg) event reducing BP threshold. Furthermore, half of BP values do not even match the looser ($<$130/85mmHg) threshold for normal BP values. This data underline the wide gaps still existing in achieving target blood pressure levels in real-life subjects.
Keywords: mobile Health; home BP monitoring

P-12

Ambulatory

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Purpose: The purpose of this study was to determine the effect of caffeine on systolic and diastolic pressure, pulse pressure and dipping pattern in a group of medicine residents who were normotensive without antihypertensive medications performing overnight duty.
Methods: We studied 10 healthy medical residents with an ultralight ambulatory blood pressure monitor (Ref: 90217A-1 Spacelabs Healthcare©) during their overnight duty averaging 8 hours. One set of recordings was performed allowing caffeine consumption through the night, while the second set of recordings was conducted without any caffeine intake during a similar night duty.
Results: There was no significant effect of caffeine on the systolic and diastolic pressure, pulse pressure, and nocturnal dipping pattern in medicine residents working overnight duty.