INTRODUCTION FROM THE PRESIDENT

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Welcome to another edition of Hypertension News. As this year comes to a close, one can reflect on what has been a significant year in the field of hypertension. There have been new guidelines from the European Society of Hypertension (ESH) issued in June, and by now you should have just about finished reading them! It is a weighty document and my colleagues at ESH, and Giuseppe Mancia and Reinhold Kreutz in particular, have completed a mammoth task in generating a useful reference source, in which somewhat ironically the volume of information is inversely related to the amount of change in guidance. This is perhaps a good thing, and is telling us that we are reaching a consensus on many of the key areas of clinical practice guidelines. That said, as commented on by Franz Messerli in this issue of Hypertension News, there remains controversy about the decision of the ESH to give more prominence to beta-blockers beyond guideline directed indications. I suspect this is a controversy that will run and run.

Another interesting area of debate has been the role of renal denervation in the treatment of hypertension. It seems such a long time ago, and certainly more than 10 years ago since I was first approached about participating as an investigator in one of the first renal denervation trials. It has been a roller coaster journey since then but only a few weeks ago, the US FDA first approved the Paradise Ultrasound Renal Denervation system from RECOR Medical and Otsuka Medical Devices, followed only 10 days later by the approval of MEDTRONIC's Symplicity Spyral renal denervation system. Both devices approved for the treatment of hypertension. It has been a long haul characterised by admirable persistence and it is going to be interesting to see where these technologies will land in the hierarchy of hypertension treatments.



Another area of development this year has been the explosion of cuffless devices that claim to "measure" blood pressure. There has been a major increase in all manner of devices advertised for sale online to consumers. Obviously, the availability of such technology would be a major breakthrough in terms of convenience and duration of blood pressure monitoring, but only if they work. Whether they work being a very important consideration. Firstly, it is important to note that these "devices" don't measure blood pressure, they estimate it using algorithms, usually based on analysis of a pulse wave form calibrated to the wearer's conventionally measured blood pressure. Second, there is very little, if any regulatory oversight of these devices, in some cases with the devices promoted by medical professionals, or even non-medical advocates, who often have no idea if, or how they work. There clearly needs to be an independent review and source of trusted information of where this technology is at, what it is capable of doing, and what it cannot do. Of course we welcome and must not stifle innovation but the measurement of blood pressure is such an important aspect of health care, this is no place for gimmicks, only facts will do. To this end, I have asked one of our Council members Professor Kario to lead a focus group of experts to generate a state of the art report of what we know about the various means by which these cuffless devices aim to measure blood pressure, whether the data justifies their claims and what the future might hold, in the face of major technological and data science advances, for blood pressure measurement and its regulation.

Finally, one cannot fail to be excited about re-emergence of interest in developing new therapeutic approaches for the treatment of hypertension. In the past year, we have seen the emergence of at least three major new therapeutic approaches; (i) The development of three new

highly selective aldosterone synthase inhibitors entering into phase 2 and 3 trials, initially for the treatment of resistant or difficult to control hypertension (baxdrostat - AstraZeneca and Larundrostat - Mineralys). This coincides with the recognition that undetected aldosteronism undoubtedly plays an underappreciated role in the genesis of hypertension and organ damage. A third aldosterone synthase inhibitor from Bayer (BI 690517) was recently evaluated in combination with an SGLT2-inhibitor in patients with chronic kidney disease. One could anticipate such a combination of aldosterone synthase inhibition with SGLT1-inhibitors being attractive for the treatment of hypertension, and in patients with chronic kidney disease, diabetes, and heart failure. (ii) The second attractive development is in the field of RNA therapeutics, specifically the use of RNA silencing (Zilebesiran, from Alnylam) to inhibit the transcription of angiotensinogen (AGT) in the liver, AGT being the key substrate for renin angiotensin system activation. A single subcutaneous injection of Zilebesiran suppressed circulation AGT by over 90% and lowered blood pressure in adults with mild-to-moderate hypertension for up to six months. With adherence to therapy being a major issue in controlling blood pressure, this extraordinary duration of action could be a major asset. Furthermore, this whole field of RNA silencing holds great promise for the treatment of many conditions where it would be desirable

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to knock down the synthesis of a single protein manufactured by the liver. Although, I suspect a reversal agent also needs to be developed. (iii) The third novel development is another approach using a biologic, specifically a humanised monoclonal antibody that specifically targets neuropeptide receptor 1 (NPR1) which is the receptor activated by atrial and brain natriuretic peptides. This approach will produce long-lasting stimulation of the NPR1 receptor, for weeks, with all the attendant potential cardiovascular benefits. Two molecules are in development (Novartis and Regeneron) and mindful of the impressive results in hypertension and in heart failure with sacubitril:valsartan, these conditions are the natural targets for early phase ongoing trials with these agents.

It is going to be fascinating to follow the progress of these new therapeutic developments for the treatment of hypertension and associated comorbidities.

So, it has been an exciting year of change and advances in the field of hypertension. We will continue to feature new developments in the field in future issues of Hypertension News but for the moment, enjoy this new edition, packed with news and information and wherever you are in the world, on behalf of the ISH, I wish you all a happy, healthy and hopefully peaceful 2024.

