

HYPERTENSION IN THE ELDERLY

ASOMEX

...delivering the chiral benefits



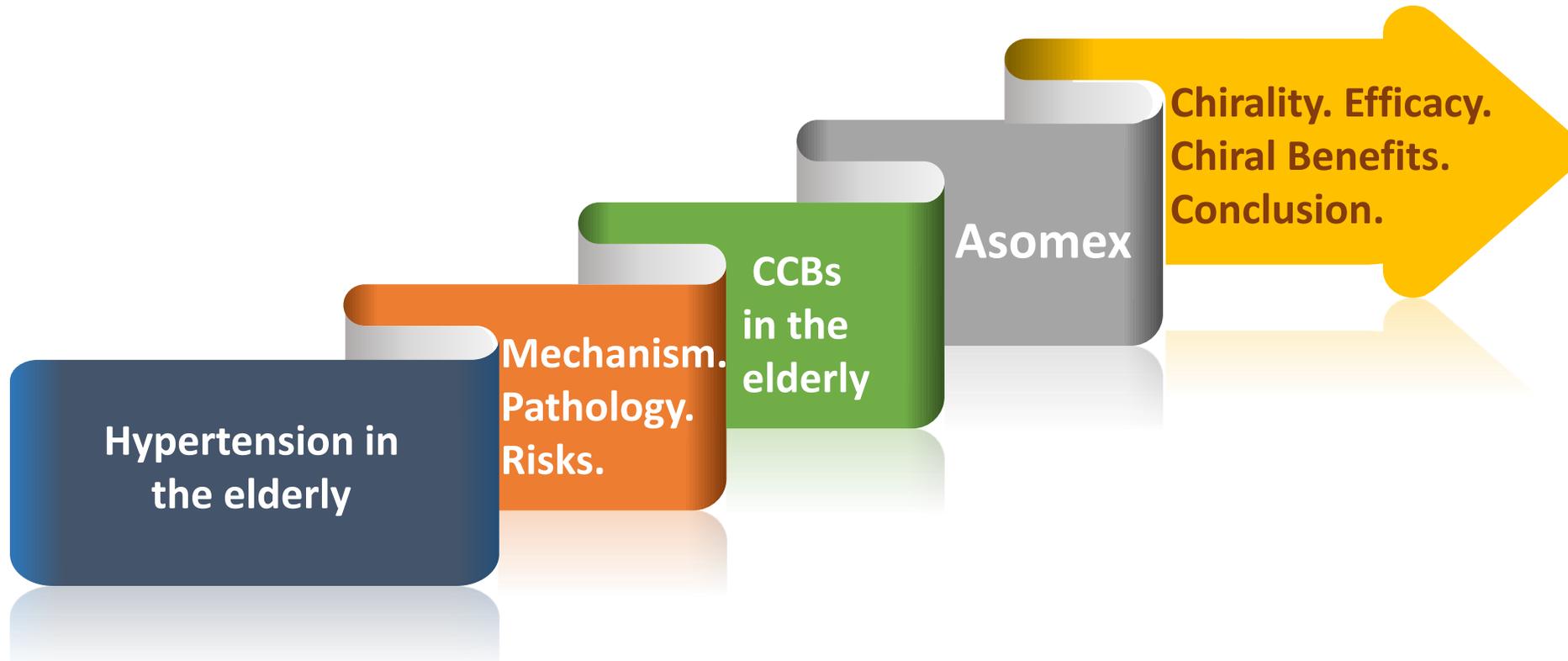


Fidson Healthcare Plc

...We value life

- **Indigenous**
- **Industry Leader**
- **Manufacturing**
- **Marketing**
- **FMCG**
- **NIS ISO 9001:2008**
- **Tested & Trusted**

Overview



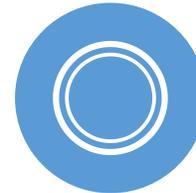
Hypertension in the elderly



Global increases in life expectancy have led to a high population of elderly people and created treatment challenges for those with HTN



Challenges of treating elderly patients to clinical goals



High economic burden of CV events: MI, HF, stroke



Greater need to improve treatment outcomes and reduce costs

Hypertension in the elderly

JNC 7

Hypertension occurs in more than two thirds of individuals >65yrs of age

90% of persons who are normotensive at 55 yrs will develop hypertension in their remaining lifespan

Framingham Heart Study

SHEP Study

ISH is age-related; Increased ISH leads to an increase in pulse pressure, a strong predictor of CV death

SHEP: Systolic Hypertension in the Elderly Program

- 1.Christensen K. et al. Ageing population: the challenges ahead. The Lancet, 2009; Vol. 374(9696):1196-1208
- 2.Fagard R.H. "epidemiology of hypertension in the elderly" Am J Geriatric Cardiol. 2002; Vol 11 (1): 23-28
- 3.Chobanian AV et al. The JNC 7 report. JAMA 2003;289:2560-2572
4. SHEP Cooperative Research Group. JAMA. 265: 3255 -3264

Pathology

Sodium sensitivity increases with age.

Due to declining ability to shed sodium overload. Raises blood volume, impairs nitric oxide production and worsens arterial stiffness.

Arterial stiffness increases

Due to endothelial dysfunction, caused by free radicals. Arterial stiffness impairs vasodilatation, which raises BP.

Isolated Systolic Hypertension increases

In the elderly, ISH is more frequent than systolic – diastolic hypertension. ISH portends a great risk of death.

White Coat Effect (WCE)

The elderly are more sensitive to being at the clinic; With WCE, patients may have SBP ≥ 140 mmHg or DBP ≥ 90 mmHg, or both

1. De Wardener H.E. et al. Sodium and BP. *Curr Opin Cardiol.* 2002;17:360-367
2. Bagrov A.Y et al. The dietary sodium-blood pressure plot “stiffens”. *hypertension.* 2004;44:22-24
3. Franklin SS. Arterial stiffness and hypertension. *Hypertension.* 2005;45:349–351
4. Vasan SV. Pathogenesis of elevated peripheral pulse pressure. *Hypertension.* 2008;51:33–36

Treatment Considerations

Elderly Hypertensive Patients.....

Are more prone to ISH than younger adults

Are more sensitive to salt intake compared to a younger population, leading to higher SBP and Pulse Pressure

Are at increased risk of developing orthostatic hypotension, syncope, falls, and injuries

Benefits of Treatment

Reports of Landmark Studies

Syst-Eur Vascular Dementia
Project (Syst-Eur)



Medical Research Council
(MRC) trial



The Systolic Hypertension in
the Elderly Program
(SHEP) trial



Conclusion

Reducing SBP in older persons
with Isolated Systolic
Hypertension (ISH) reduced
morbidity and mortality.



CCBs are effective in the elderly

Several therapeutic options exist but the DHP-CCBs are preferred

JNC 8 recommends CCBs (or diuretics) as 1st line therapy in the elderly because of age-related differences in the mechanism of HTN

CCBs are suitable for elderly patients with ISH.
(European Society for Hypertension)



Starting therapy with a DHP-CCB improves prognosis in the elderly with ISH.

(The Systolic Hypertension in Europe (Syst-Eur) Study)

CCBs have no metabolic effect: an advantage over diuretics in the elderly, in whom the metabolic syndrome is common.

Compared to other HTN drugs, DHP-CCBs have a high hypotensive efficacy without affecting organ blood flow; thus effective in the elderly

CCBs are effective in the elderly

Most physicians prefer CCBs as their drug of 1st choice:

- HTN without comorbidities:

53.8% of physicians

- HTN with CKD:

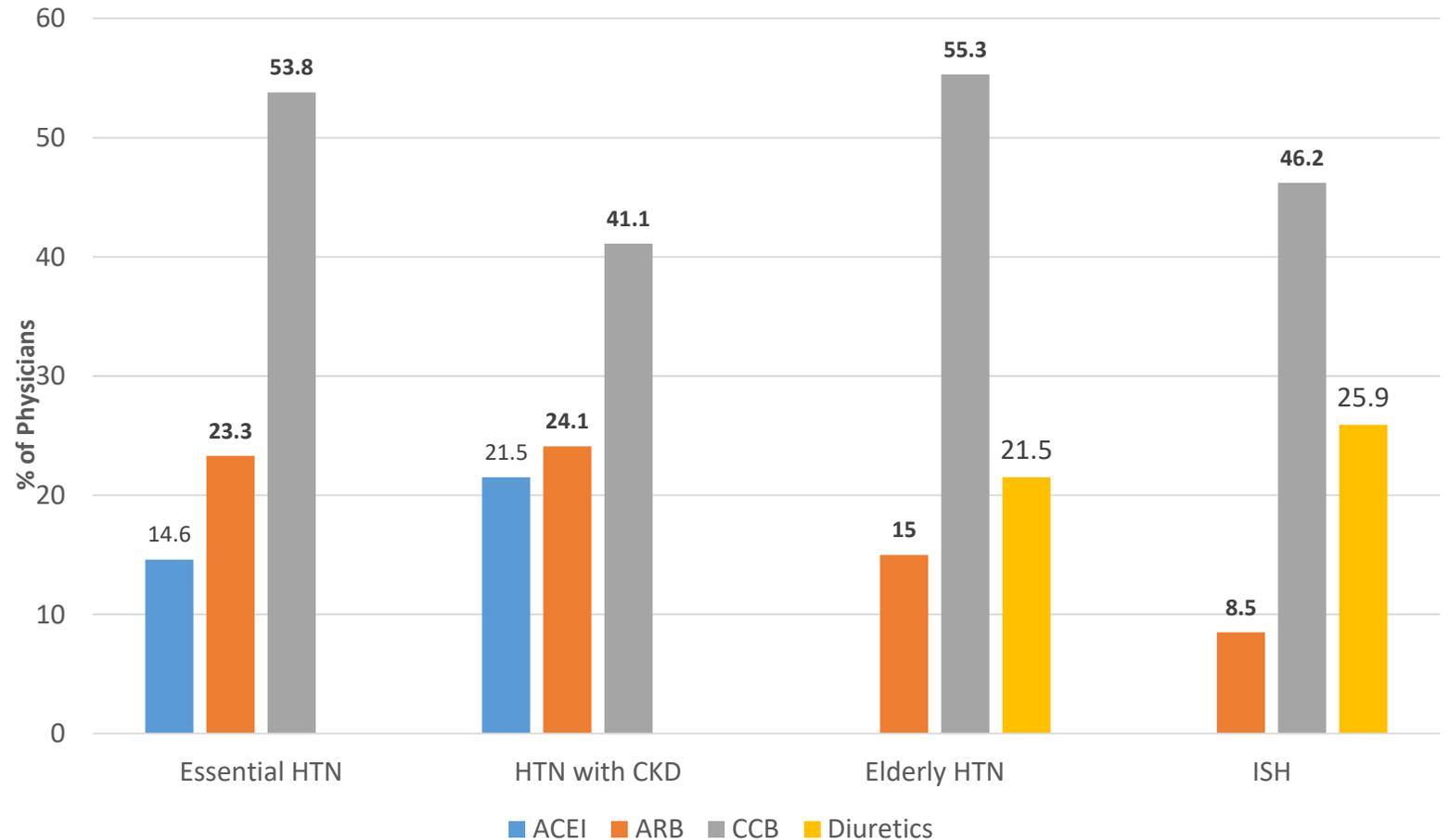
41.1% of physicians

- Elderly patients with HTN:

55.3% of physicians

- Isolated Systolic HTN:

46.2% of physicians



Introducing **Asomex**



.....delivering the chiral benefits



Molecular Chirality



Asomex is a DHP-CCB, but differs from other CCBs via the concept of chirality



The parent compound, Amlodipine, is a racemic mixture of S and R enantiomers

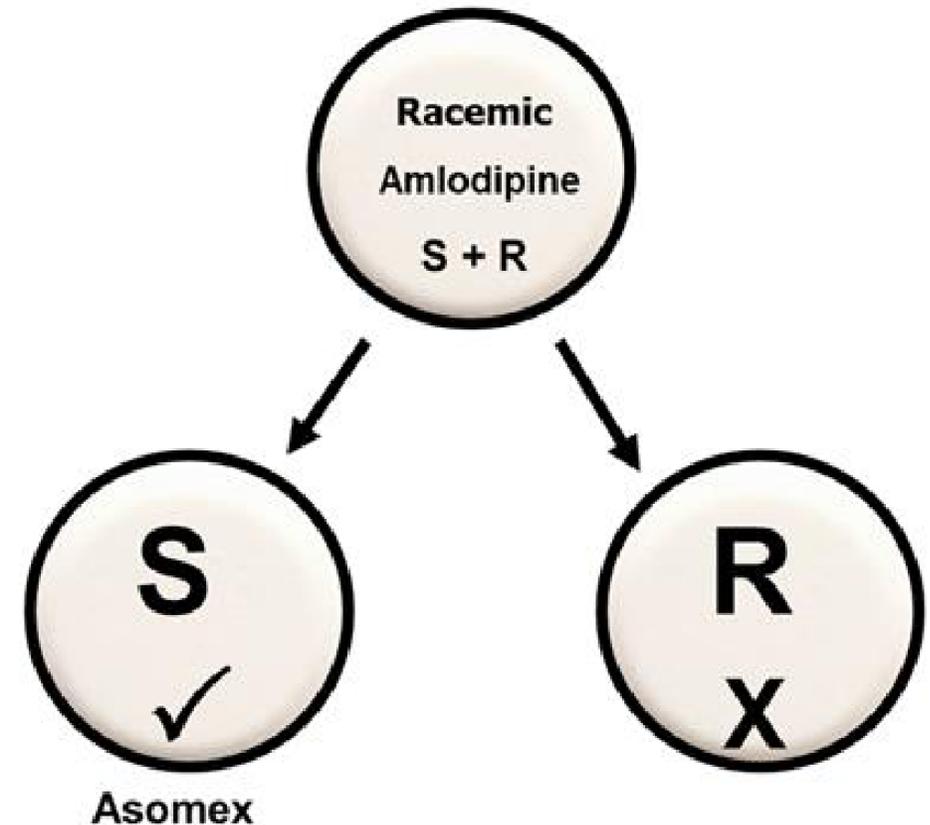


The S-enantiomer has a 1000-fold greater affinity for DHP receptors than the R-enantiomer



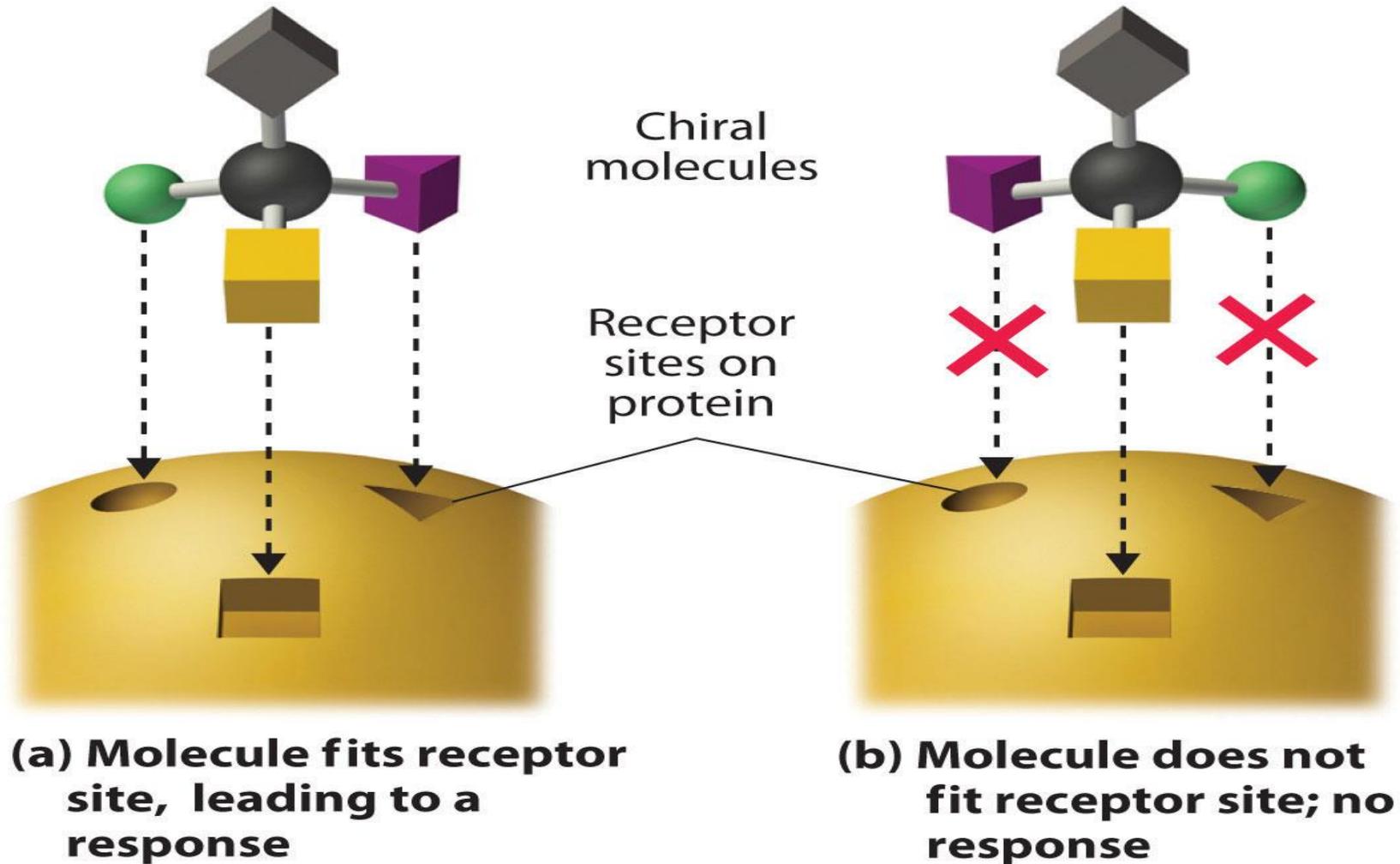
The S-enantiomer is responsible for the vasodilating effect of Amlodipine.

Asomex is the chirally pure S-enantiomer.



Molecular Chirality

Drug-Receptor Interaction



Molecular Chirality

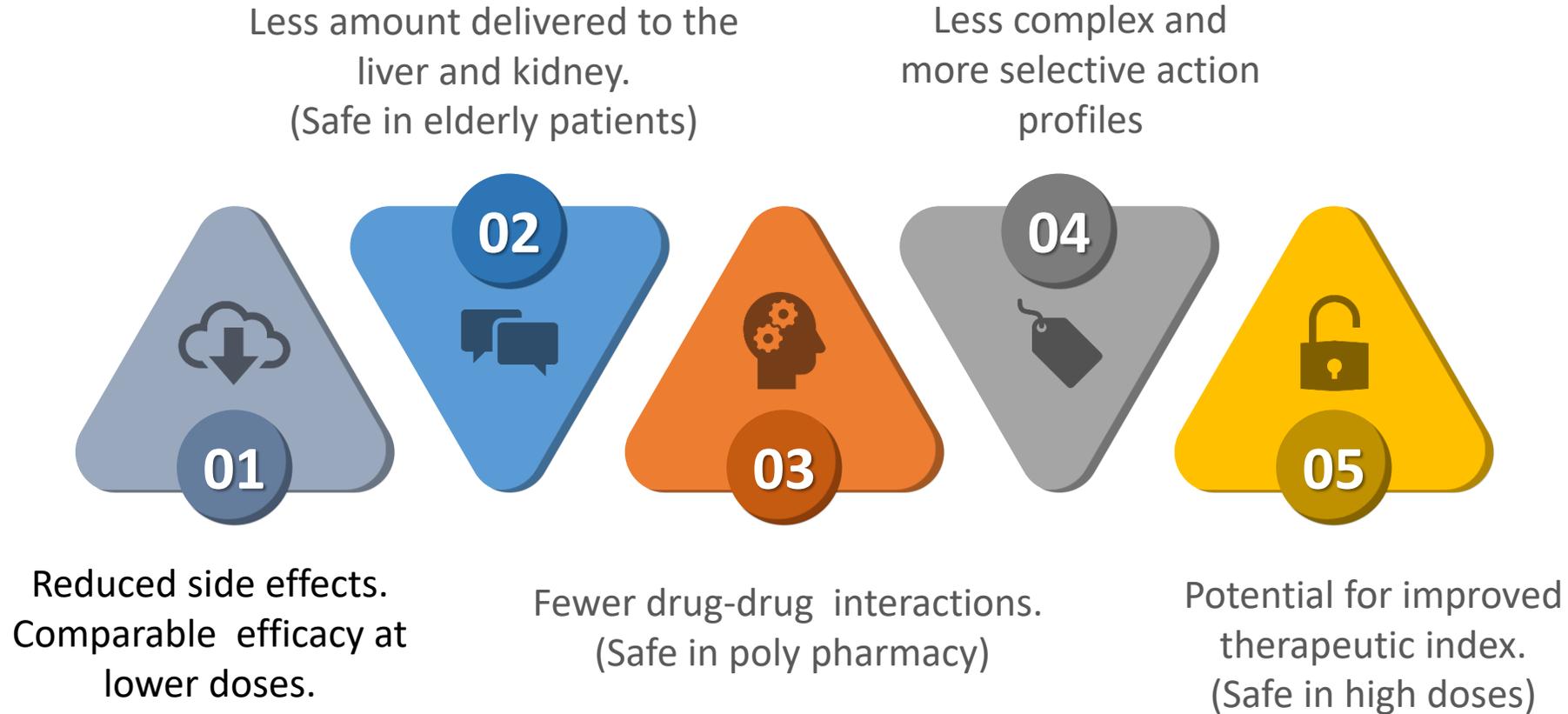
S-Amlodipine

- Protects the heart and the coronary arteries
- Responsible for the anti angina effects of Amlodipine
- Has much lower incidence of peripheral edema compared to racemic amlodipine
- Has better overall safety profile

R-Amlodipine

- Inactive but may not be completely inert
- Responsible for local changes that lead to peripheral edema

Advantages of chiral purity



Chiral Switch

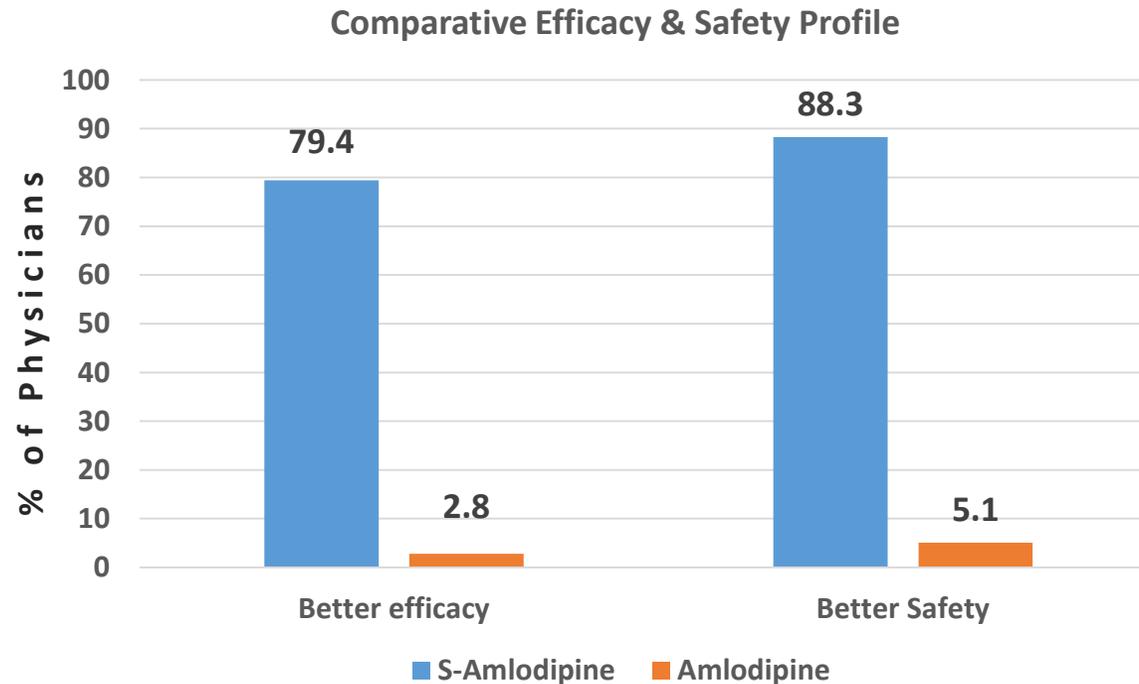
Racemic Amlodipine to S-Amlodipine



“The introduction of S-Amlodipine is a step in the right direction. It would make sense to perform a chiral switch in the management of HTN to avoid the potentially harmful effects of the R-isomer in the racemates”

Efficacy

Physicians' Preference



More physicians prefer S-Amlodipine to racemic Amlodipine because of better efficacy and safety profile

Efficacy

Asomex in the elderly

MICRO – SESA II

Description: A sub group analysis of the SESA study.

Objective: To determine the efficacy & safety of S-Amlodipine in the treatment of HTN in the elderly

Result : With a population size of 339, overall responder rate was 96.46%. In 33 patients with concomitant DM, reductions in SBP and DBP were higher and responder rate was 100%

Conclusion: S-Amlodipine is effective, safe and well tolerated in the treatment of HTN in the elderly.

SESA = Safety & Efficacy of S-Amlodipine

Efficacy

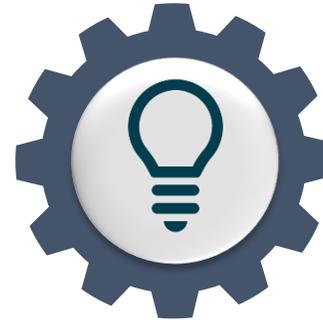
Asomex Landmark Studies

Study	Objective	Conclusion
Safety & Efficacy of S-Amlodipine (SESA)	Evaluate the efficacy & safety of S-Amlodipine in HTN	S-Amlodipine is effective in hypertension therapy. Ideal switch for patients having pedal edema with Amlodipine.
SESA-Angina Study	Evaluate the efficacy & safety of S-Amlodipine in angina	S-Amlodipine is effective, safe and well tolerated in the treatment of angina
Micro-SESA 1	Evaluate the efficacy & safety of S-Amlodipine in ISH	S-Amlodipine is effective & safe in the treatment of ISH grades I & II, without any side effects.
SESA IV	Evaluate the efficacy of S-Amlodipine in Stages I & II HTN	S-Amlodipine is effective, safe & well tolerated in the treatment of patients with stages I & II HTN.

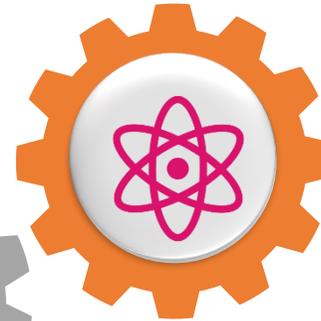
1. SESA Study Group. JAMA 2003;Vol. 2(8):87-92
2. Jagdish Hiremath, India Medical Gazette. 2005; CXXXIX():403-408
3. SESA Study group. Indian Medical Gazette. 2005; CXXXIX(6):343 – 358
4. SESA IV Study group. Cardiology Today. 2007. Vol. XI. No.5.

Safety & Tolerability

CCBs are associated with a risk of peripheral edema that may reduce medication compliance or necessitate switching to a different drug



Incidence of pedal edema is 20% less with **Asomex** compared to racemic Amlodipine



When patients on racemic Amlodipine with pedal edema were switched to S-Amlodipine, 98.72% of cases were completely resolved

The ASCOT-BPLA reported that 1 out of 4 patients on Amlodipine may develop pedal edema



ASCOT-BPLA: Anglo-Scandinavian Cardiac Outcomes Trial-BP Lowering Arm

SESA Study Group. JAMA. 2003; Vol 2(8): 87-92

B. Dahlöf, et al., The Lancet, 2005; vol. 366 (9489):895-906

Rahimi et al. Circulation Research, 2015; vol. 116(6):925-935

Oke D.A et al. Comparative cross over trial of S-Amlodipine besylate and Amlodipine besylate in the treatment of mild to moderate HTN. Feb., 2008



Safety & Tolerability

In SESA Trial

- Pedal edema was resolved in 98.72% of patients after switching from the racemic amlodipine to S-Amlodipine

In SESA II Study

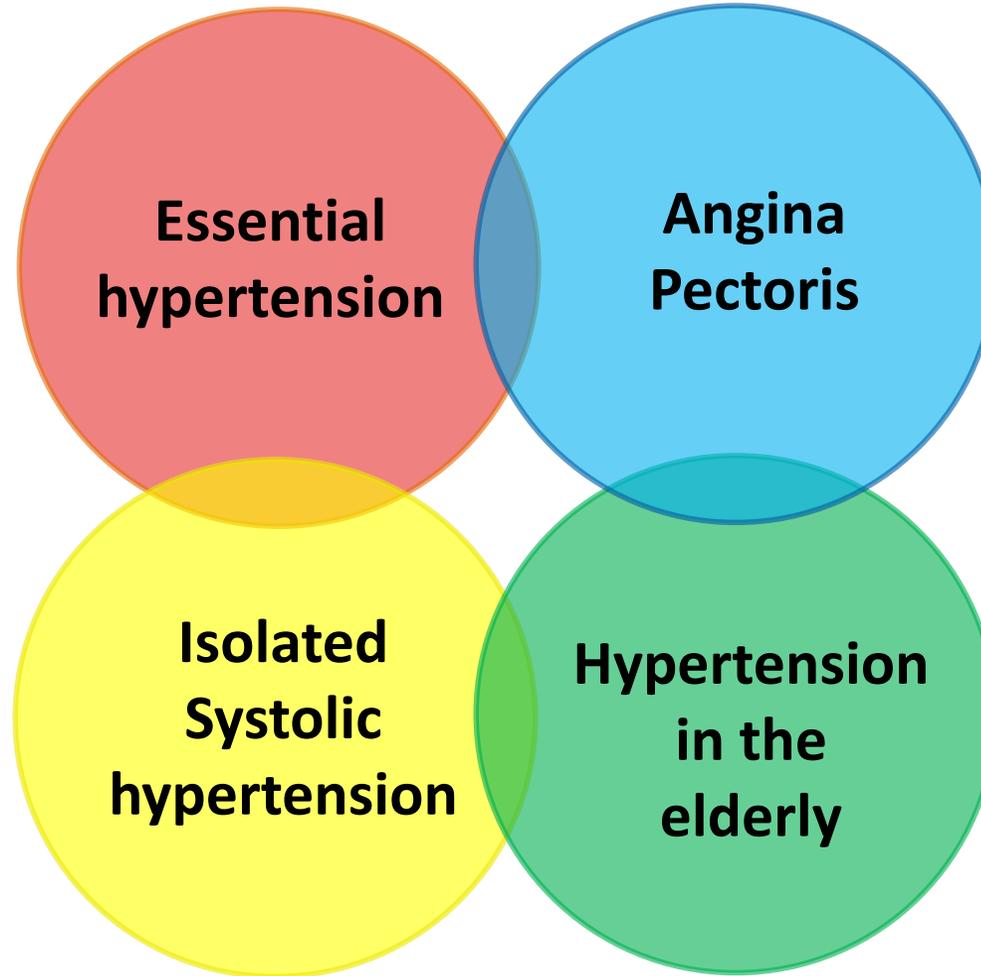
- Pedal edema was reported in 41.90% of patients taking racemic amlodipine, but was resolved when switched to S-Amlodipine

In the Asomex Comparative Cross Over Trial

- Overall safety and tolerability profile was better with **Asomex** (S-Amlodipine) than the racemic Amlodipine

Evidence convincingly shows that S-Amlodipine is safer and more tolerable than racemic Amlodipine

Indications



Dosage

**2.5mg to 5mg,
Once Daily**

The chiral benefits

S/n	Feature	Benefits
01	Low incidence of pedal edema & headache	Improved compliance and optimal BP control
02	Longer half life (49.6hr)	Better round-the-clock BP reduction
03	Greater efficacy at lower doses	No hepatic drug overload in the elderly
04	Reduced inter individual variability in drug response	Predictable treatment outcome
05	Reduced potential for drug-drug interaction	Safety in concomitant therapy in comorbid conditions

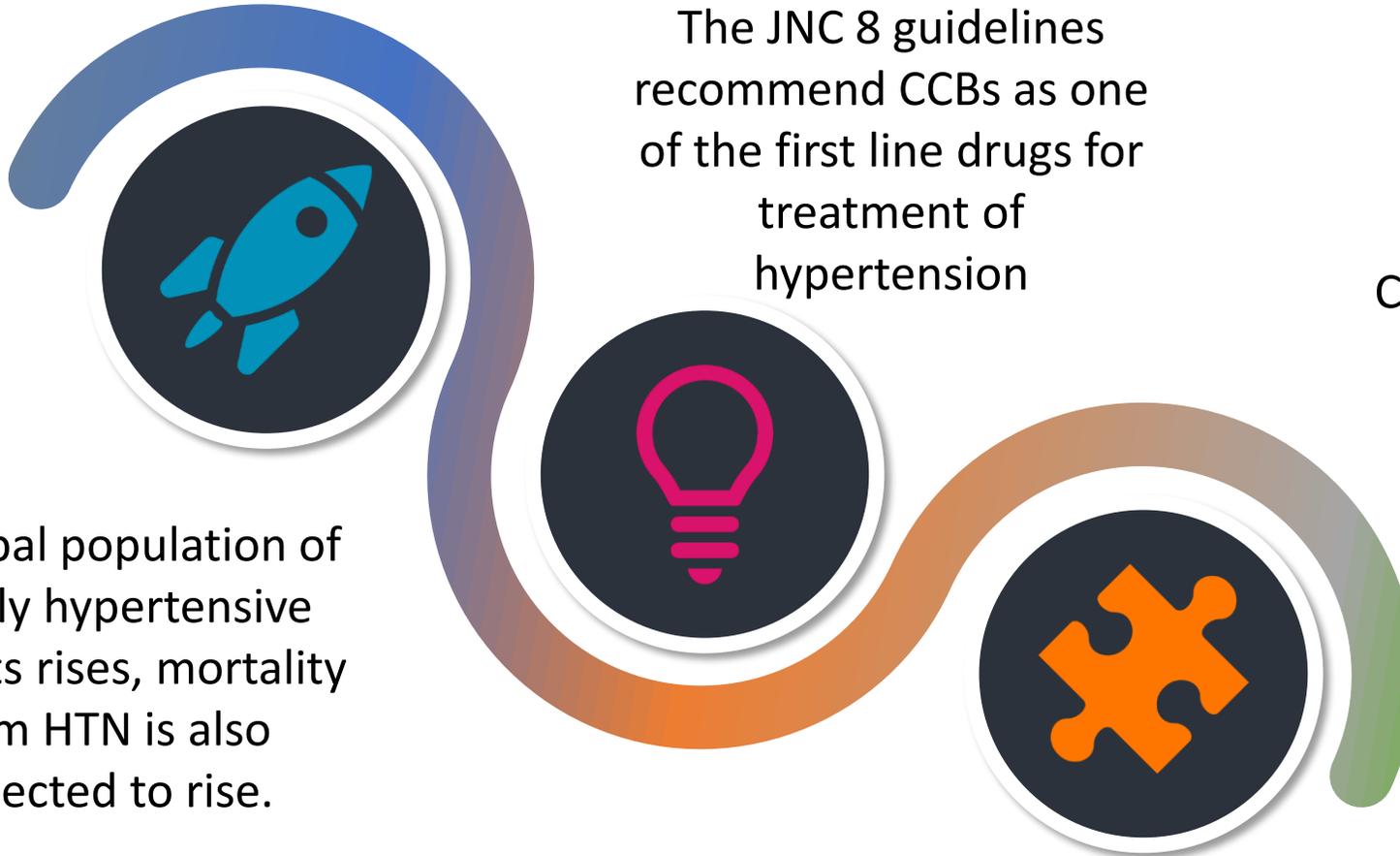
Conclusion



The JNC 8 guidelines recommend CCBs as one of the first line drugs for treatment of hypertension



European Society of Cardiology (ESC) & European Society of Hypertension (ESH) also recommend a long-acting DHP-CCB for elderly patients with ISH.



As global population of elderly hypertensive patients rises, mortality from HTN is also expected to rise.



Brand Promises

Asomex.....

Delivers the benefits of chiral purity

04

01

Protects the heart and the coronary arteries

Has no metabolic effects, but improves quality of life of elderly hypertensive patients

03

02

Is effective, safe and well tolerated in the treatment of HTN in the elderly



THANK YOU