Sacubitril-valsartan: novel therapy for heart failure

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Clinical question

Is sacubitril-valsartan effective for systolic heart failure (HF)?

Bottom line

If 36 patients with HF are switched from angiotensin-converting enzyme inhibitors (ACEIs) to sacubitril-valsartan, 1 fewer dies and 1 fewer is admitted for HF over 27 months. Aldosterone antagonists and β-blockers should be given first and continued concurrently.

Evidence

- In 1 RCT,[1] 8399 patients with systolic HF (mean age 64, about 94% class II or III, B-type natriuretic peptide [BNP] level about 250 ng/L, about 7% North American) switched from ACEIs to sacubitril-valsartan (200 mg) twice daily or enalapril (10 mg) twice daily.
  -At 27 months, sacubitril-valsartan statistically significantly reduced cardiovascular death or HF hospitalization (22% vs 27%, number needed to treat [NNT]=22); cardiovascular death (13% vs 17%, NNT=32); HF hospitalization (13% vs 16%, NNT=36); all-cause mortality (17% vs 20%, NNT=36); and mean blood pressure by about 3 mm Hg. There were fewer discontinuations for renal impairment (0.7% vs 1.4%, NNT=143).
  -Adverse effects were fewer (10.7% vs 12.3%, NNT=63), but symptomatic hypotension (14% vs 9.2%, number needed to harm=20) and angioedema (19 vs 10 patients) increased.
  -Limitations of the trial: about 20% withdrew during run-in, it stopped early, and it was industry sponsored.

Context

- The usefulness of initiating therapy based on BNP levels is unknown, as most HF patients have elevated levels.[2]
- About 93% of participants were taking β-blockers and half were taking aldosterone antagonists concurrently.[1]
- Aldosterone antagonists, ACEIs, and β-blockers each reduce relative risk all-cause mortality by 20% to 30%.[3]
- Guidelines recommend replacing ACEIs or angiotensin receptor blockers with sacubitril-valsartan if patients take ACEIs, β-blockers, and aldosterone antagonists with elevated natriuretic peptide levels or were hospitalized for HF in the past 12 months.[4,5]
- Initial dose is 50 to 100 mg twice daily with possible titration to 200 mg in 2 to 4 weeks.[6] About 40% need a reduction (but one-third are able to return to the full dose).[7]
- Although not covered by many insurance plans, it is a recommended benefit.[8] Cost is about $250 per month.

Implementation

To switch between sacubitril-valsartan and ACEIs, a 36-hour washout is recommended to prevent angioedema.[6] The valsartan in the 50-, 100-, and 200-mg combinations is equivalent to common valsartan doses of 40, 80, and 160 mg.[6] Sacubitril-valsartan might have stronger diuretic and natriuretic effects than valsartan alone,[9] and blood pressure, fluid status, and diuretic dose should be monitored. Sacubitril-valsartan raises BNP levels. If natriuretic peptide measurement is needed, N-terminal pro-BNP level is preferred, as it is not affected by sacubitril-valsartan.[6]

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Competing interests
None declared

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