# [Early Experience With Sacubitril/Valsartan in Adult Patients With Congenital Heart Disease.](https://www.ncbi.nlm.nih.gov/pubmed/31084317)

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**Take Home Points:**

1. Congestive heart failure due to systolic heart dysfunction in ACHD patients is a common cause of early death and disability. Many medications in the general population have copious evidence of improving outcomes in the general CHF population; however ACHD has very little evidence of any drugs working due to patient heterogeneity, small sample sizes, limited follow-up, and other issues that make a well-designed clinical trial very hard to execute.
2. Sacubitril/valsartan is a newer FDA-approved drug in a new class known as an ARNI. It combines an angiotensin II receptor blocker (ARB) with a neprilysin inhibitor (NI). This combination affects both the renin-angiotensin-aldosterone system (RAAS) and the natriuretic peptide (NP) systems. This drug showed ~20% reduction in mortality compared to standard therapy in the PARADIGM-HF trial, with over 8000 patients randomized.
3. There is limited evidence that drugs affecting the NP system may improve symptoms in patients with pulmonary hypertension and/or systemic right ventricles, which are both commonly encountered in ACHD.
4. To date, there has been very little study of ARNI in ACHD. This paper is the 2nd of 3 published to evaluate this topic. This paper had 15 patients; the first paper had 4 and the most recent 23 patients under study.
5. The study was underpowered to show statistically significant results but did demonstrate anecdotal improvement in 4/5 patients with NYHA class III symptoms and also only 1/15 (6.6%) had to stop the medication (the rate of stopping the medication was 10.7% in PARADIGM-HF)



***Commentary from Dr. W. Aaron Kay (Indianapolis), section editor of ACHD Journal Watch:***

**Although most congenital defects can be repaired with excellent survival to adulthood, congestive heart failure due to significant systolic dysfunction is often a common final pathway leading to early disability and death in ACHD patients. Sacubitril/valsartan, a unique drug in a novel class known as ARNIs (angiotensin receptor inhibitor combined with a neprilysin inhibitor) has recently entered the armamentarium of heart failure drugs, and although there hasn't been a lot of long-term experience with it, it has been studied in the largest heart failure trial ever, in terms of sheer volume of patients, in the PARADIGM-HF trial, which randomized over 8000 patients to ARNI versus enalapril. That trial, in the general non-ACHD population, showed significant superiority of ARNI over enalapril; however to date there has been very little formal study of ARNI usage and outcomes in the ACHD population.**

**This small retrospective review coming from University of California Los Angeles (UCLA) shows the entirety of their first year experience using sacubitril/valsartan. Patients included a variety of anatomic congenital heart diagnoses (2 Fontans, the rest with 2-ventricle repairs); all patients had either NYHA II or NYHA III symptoms at baseline. Of the 15 total patients on the medication, 14 were able to tolerate it (one stopped due to renal failure). In the PARADIGM-HF trial, ~10.7% of patients had to stop ARNI due to side effects, most commonly hypotension and hyperkalemia.**

**The number of patients was very low, in one of the largest ACHD centers in the United States, which likely reflects the ACHD community's general reluctance to try new drugs until they have been proven safe in the larger non-CHD community, as well as issues of expense - most ACE inhibitors are available even without insurance for $4 a month, whereas sacubitril/valsartan costs more than $1000 a month without insurance.**

**The study presented here was retrospective, and too small to have adequate power to draw meaningful statistical conclusions. However, it is notable that that 4/5 patients with NYHA class III CHF symptoms had improvement in their degree of heart failure symptoms. Mechanistically, it stands to reason that patients with 2-ventricle repairs and a subaortic left ventricle would be similar to the general heart failure population studied in PARADIGM-HF; however ACHD has been plagued by lack of large enough trials to prove or disprove that ACE inhibitors, ARBs, and other heart failure drugs make a significant difference in those with systemic right ventricles or single ventricles.**

**This study is quite interesting, and perhaps when the price of sacubitril/valsartan comes down more it will be adopted more commonly in ACHD versus cheaper alternatives. Given the lack of evidence of heart failure drugs in general in ACHD, as well as the robustness that ARNI appears to be superior to ACE in PARADIGM-HF, the authors appropriately call for a large multicenter trial by the US/Canada -based Alliance for Adult Research in Congenital Cardiology (AARCC) to be performed on a prospective basis, as we have a multitude of ACHD patients suffering premature death due to systolic ventricular dysfunction despite good repairs as children, thus more evidence that ARNI can alleviate that burden will be very helpful.**

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