Appendix 4. Supplemental Clinical Data

Primary Effectiveness Endpoint for 3 studies for multiple cohorts

Table 4.1 shows the change in daytime ASBP for the Intent to treat (ITT), per protocol (PP), and complete ABP (CA) patient populations in each of the three studies.

Table 4.1. Primary Effectiveness Endpoint for RADIANCE-HTN Studies, Daytime Ambulatory SBP (mmHg) - ITT, PP, CA

	uRDN			**Sham**			**Baseline Adjusted**	
	Baseline	**2 months**	**Change**	**Baseline**	**2 months**	**Change**	**Mean/Median Difference (95% CI) (uRDN - Sham)[1]**	**p-value[1]**
SOLO								
ITT uRDN = 74 Sham = 72	150.3 ± 7.8 149.1 [134.8, 165.8]	141.9 ± 11.9 140.6 [113.3, 166.7]	-8.5 ± 9.3 -8.5 [-28.9, 13.6] (-10.6, -6.3)	150.0 ± 9.8 150.1 [134.5, 176.7]	147.9 ± 13.3 147.7 [118.1, 177.4]	-2.2 ± 10.0 -1.1 [-34.2, 25.0] (-4.5, 0.2)	-6.3 [-9.4, -3.1]	0.0001
PP uRDN = 64 Sham = 58	150.5 ± 7.3 149.6 [134.8, 165.7]	142.0 ± 11.7 141.0 [113.3, 166.7]	-8.5 ± 9.6 -8.6 [-28.9, 13.6] (-10.9, -6.1)	149.5 ± 9.9 148.8 [134.5, 176.7]	149.4 ± 12.0 148.7 [124.0, 177.4]	-0.1 ± 8.5 -0.8 [-22.2, 25.0] (-2.3, 2.1)	-8.2 [-11.5, -5.0]	<.0001
CA uRDN = 73 Sham = 71	73 150.5 ± 7.7 149.4 [134.8, 165.8]	73 141.9 ± 12.0 140.6 [113.3, 166.7]	73 -8.6 ± 9.3 -8.7 [-28.9, 13.6] (-10.7, -6.4)	71 149.9 ± 9.8 150.1 [134.5, 176.7]	71 147.7 ± 13.3 147.6 [118.1, 177.4]	71 -2.2 ± 10.1 -1.2 [-34.2, 25.0] (-4.6, 0.2)	-6.3 [-9.5, -3.1]	0.0001
TRIO								
ITT uRDN = 69 Sham = 67	150.0 ± 11.9 147.1 [134.5, 179.8]	141.0 ± 16.1 138.6 [105.8, 193.2]	-9.0 ± 14.5 -8.0 [-61.3, 26.0] (-12.5, -5.5)	151.1 ± 12.6 148.8 [133.8, 202.0]	146.3 ± 18.8 143.0 [107.6, 200.7]	-4.8 ± 15.9 -3.0 [-67.9, 47.9] (-8.6, -0.9)	-4.5 [-9.6, 0.6] -4.5 [-8.5, -0.3][2]	0.0809 (0.0223*)

	uRDN			Sham			Baseline Adjusted	
	Baseline	**2 months**	**Change**	**Baseline**	**2 months**	**Change**	**Mean/Median Difference (95% CI) (uRDN - Sham)[1]**	**p-value[1]**
PP uRDN = 55 Sham = 57	149.9 ± 12.4 145.7 [134.5, 179.8]	140.8 ± 17.6 138.6 [105.8, 193.2]	-9.1 ± 14.8 -8.7 [-61.3, 26.0] (-13.2, -5.1)	150.2 ± 12.3 147.5 [134.8, 202.0]	145.1 ± 19.0 142.4 [107.6, 200.7]	-5.1 ± 15.9 -3.3 [-67.9, 47.9] (-9.3, -0.9)	-4.1 [-9.8, 1.7] -5.4 [-9.5, -1.3][2]	0.1614 (0.0109*)
CA uRDN = 63 Sham = 67	150.3 ± 12.3 146.8 [134.5, 179.8]	140.4 ± 16.7 137.6 [105.8, 193.2]	-9.8 ± 14.9 -9.7 [-61.3, 26.0] (-13.6, -6.1)	151.1 ± 12.6 148.8 [133.8, 202.0]	146.3 ± 18.8 143.0 [107.6, 200.7]	-4.8 ± 15.9 -3.0 [-67.9, 47.9] (-8.6, -0.9)	-5.3 [-10.6, -0.0] -5.8 [-9.7, -1.6][2]	0.0491 (0.0051*)
RADIANCE-II								
ITT uRDN = 145 Sham = 73	150.2 ± 8.6 149.0 [135.0, 169.0]	142.3 ± 13.4 140.0 [104.0, 183.0]	-7.9 ± 11.6 -8.0 [-41.0, 26.0] (-9.8, -6.0)	151.3 ± 9.0 151.0 [136.0, 170.0]	149.5 ± 11.1 149.0 [127.0, 176.0]	-1.8 ± 9.5 -1.0 [-30.0, 26.0] (-4.1, 0.4)	-6.3 [-9.3, -3.2] -7.0 [-9.0, -4.0][2]	<.0001 (<.0001*)
PP uRDN = 131 Sham = 63	149.8 ± 8.5 148.0 [135.0, 169.0]	141.9 ± 13.4 139.0 [104.0, 183.0]	-7.9 ± 11.7 -9.0 [-41.0, 26.0] (-9.9, -5.9)	150.0 ± 8.3 148.0 [136.0, 168.0]	149.0 ± 10.8 148.0 [127.0, 176.0]	-1.0 ± 9.0 -1.0 [-22.0, 26.0] (-3.3, 1.3)	-6.9 [-10.2, -3.6] -7.0 [-10.0, -4.0][2]	<.0001 (<.0001*)
CA uRDN = 145 Sham = 73	150.2 ± 8.6 149.0 [135.0, 169.0]	142.3 ± 13.4 140.0 [104.0, 183.0]	-7.9 ± 11.6 -8.0 [-41.0, 26.0] (-9.8, -6.0)	151.3 ± 9.0 151.0 [136.0, 170.0]	149.5 ± 11.1 149.0 [127.0, 176.0]	-1.8 ± 9.5 -1.0 [-30.0, 26.0] (-4.1, 0.4)	-6.3 [-9.4, -3.2] -7.0 [-9.0, -4.0][2]	<.0001 (<.0001*)

Data displayed as Mean±SD, Median [Range], and 95% CI for change. Change is calculated as 2 months - Baseline

[1]Mean difference with 95% CI and p-value value from ANCOVA, adjusting for baseline value. In the event that the change from baseline in either cohort is non-normal, the p-value (*) from a baseline adjusted ANCOVA on the ranks is also provided.

[2]Median Difference - Hodges-Lehmann estimate of location shift and 95% asymptotic CI which are not associated with the p-value (*) via a baseline adjusted ANCOVA on the ranks

Note that all listed p-values are not adjusted for multiplicity.

Secondary Effectiveness Endpoints for TRIO – Completers population

Table 4.2 shows the secondary endpoints at 2 months of 24-hour SBP/SBP, Nighttime SBP/DBP, and Daytime DBP at 2 months for the CA population. The differences between the uRDN and Sham groups are larger than in the ITT population. The median differences in 24-hour and nighttime SBP/DBP are statistically significant, and only 24-hour ASBP were above the clinically meaningful threshold of 5.0 mmHg.

Table 4.2: Secondary Endpoint BP Change from Baseline to 2 Months (Complete 2M ABPM Population)

	Renal Denervation (n=69)			**Sham Procedure (n=67)**			**Unadjusted**	**Baseline Adjusted**	
	Baseline	**2 month**	**Difference**	**Baseline**	**2 month**	**Difference**	**Median Difference (95% CI) (uRDN – Sham)[1]**	**Mean Difference (95% CI) (uRDN - Sham)[2]**	**p-value[2]**
24 Hour Ambulatory systolic blood pressure (mmHg)	63 144.0 ± 13.9 138.8 [123.3, 180.1]	63 134.5 ± 16.4 132.5 [102.5, 194.7]	63 -9.5 ± 14.3 -9.4 [-55.2, 30.8] (-13.1, -5.9)	67 145.4 ± 14.0 142.4 [125.0, 201.6]	67 140.5 ± 18.7 138.2 [103.1, 197.2]	67 -4.8 ± 16.5 -2.9 [-62.7, 61.4] (-8.9, -0.8)	-5.6 [-9.5, -1.3]	-5.1 (-10.3, 0.1)	0.0523 (0.0043*)
24 Hour Ambulatory diastolic blood pressure (mmHg)	63 89.1 ± 8.5 87.6 [75.6, 113.1]	63 83.3 ± 11.4 81.9 [63.0, 122.5]	63 -5.7 ± 8.9 -5.6 [-34.5, 20.5] (-8.0, -3.5)	67 89.5 ± 9.5 87.2 [76.8, 131.8]	67 85.8 ± 12.0 84.6 [66.5, 125.3]	67 -3.7 ± 10.8 -2.4 [-44.5, 38.4] (-6.4, -1.1)	-2.7 [-5.3, 0.0]	-2.1 (-5.5, 1.2)	0.2141 (0.0423*)
Nighttime Ambulatory systolic blood pressure (mmHg)	63 134.1 ± 18.4 129.6 [104.7, 181.2]	63 125.2 ± 18.5 123.7 [91.2, 196.9]	63 -8.9 ± 16.3 -9.0 [-49.2, 39.2] (-13.0, -4.8)	67 136.4 ± 18.6 132.4 [100.5, 199.4]	67 131.9 ± 20.9 129.9 [89.1, 193.1]	67 -4.5 ± 19.5 -1.8 [-72.1, 77.9] (-9.3, 0.2)	-5.0 [-10.1, 0.5]	-5.3 (-11.0, 0.4)	0.0692 (0.0146*)
Nighttime Ambulatory diastolic blood pressure (mmHg)	63 81.4 ± 11.0 79.7 [60.0, 114.7]	63 75.8 ± 12.5 73.9 [54.9, 121.0]	63 -5.5 ± 10.4 -5.7 [-28.9, 23.8] (-8.2, -2.9)	67 81.3 ± 12.1 80.3 [57.9, 125.5]	67 78.4 ± 13.2 77.0 [49.4, 119.7]	67 -2.8 ± 12.9 -2.0 [-54.2, 48.3] (-6.0, 0.3)	-3.6 [-7.0, -0.1]	-2.7 (-6.4, 1.1)	0.1639 (0.0249*)
Daytime Ambulatory diastolic blood pressure (mmHg)	63 94.0 ± 7.9 91.6 [82.6, 112.6]	63 88.1 ± 12.1 84.1 [66.7, 123.8]	63 -5.9 ± 9.5 -6.0 [-39.3, 18.7] (-8.2, -3.5)	67 94.6 ± 9.1 91.6 [82.9, 136.1]	67 90.7 ± 12.2 89.5 [68.8, 137.1]	67 -3.9 ± 10.5 -2.0 [-41.7, 30.2] (-6.5, -1.3)	-2.5 [-5.4, 0.3]	-2.1 (-5.5, 1.4)	0.2367 (0.0811*)

Data displayed as Mean±SD, Median [Range], and 95% CI for change. Change is calculated as 2 months - Baseline

[1]*Hodges-Lehmann estimate of location shift and 95% asymptotic CI.*
[2]*Mean difference with 95% CI and p-value value from ANCOVA, adjusting for baseline value. In the event that the change from baseline in either cohort is non-normal, the p-value (*) from a baseline adjusted ANCOVA on the ranks is also provided.*
Note that all listed p-values are not adjusted for multiplicity.

Patient Preference Study Supplementary Data

Table 4.3 shows the patient attributes and levels for ReCor's patient preference study. Table 4.4 shows an example of a discrete choice experiment (DCE).

Table 4.3 Attributes and Levels

Attributes		**Possible Levels**	
Patients who have CV event in next 10 years		Under 55 years old	55 years old and over
		15%	30%
		30%	45%
		45%	60%
Current treatment	Number of pills per day	0 pills a day	
		1 pill a day	
		2 pills a day	
		3 pills a day	
	Minimally invasive procedure	No procedure	
		Procedure	
Patients who have mild-to-moderate side effects requiring more doctor visits		20%	
		30%	
		40%	
		50%	
		70%	
Patients who have serious side effects requiring hospitalization		0%	
		5%	
		10%	
		20%	
Patients who have serious side effects requiring a procedure		0%	
		5%	
		10%	
		No additional treatment	
Future treatments required to manage your blood pressure		Additional pill in 1 year	
		Additional pill in 3 years	
		Additional procedure in 3 years	
		Additional procedure in 7 years	

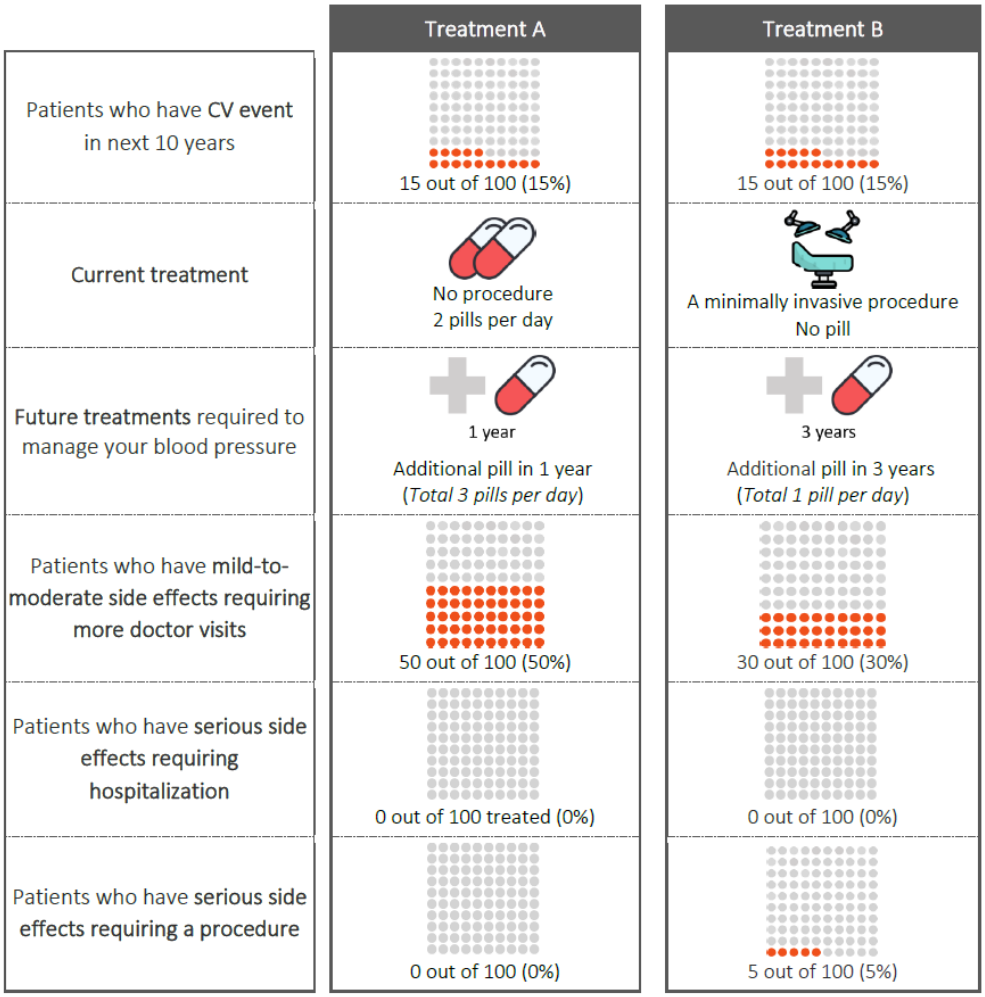

Figure 4.4. Example Discrete Choice Experiment