Six month AV Fistulae outcomes Following Local Perianastomotic Delivery of SirolimusPreliminary Report from a US Phase 3 Clinical Trial (ACCESS Trial)

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Background

AV Fistula (AVF) maturation delay impacts its functional patency and prolongs catheter dependence. USRDS (2015) reports median time to first cannulation of 112 days and only 45% of AVF are suitable for dialysis at 6 months [Range 38% (DAC) to 65% (HFM)]. A prior single arm Phase 2 study (Table) tested the value of perivascular sirolimus delivered intraoperatively at and around the AVF anastomosis from a collagen membrane (drug product; Vascular Therapies, Cresskill, NJ), for improving AVF outcomes.

Methods

Incident ESRD patients undergoing hemodialysis via catheter at time of AVF creation [Radiocephalic (RCF) or Brachiocephalic (BCF)] are eligible for enrollment in this ongoing US Phase 3 multicenter, randomized controlled clinical trial (NCT02513303). The first subject enrolled at each site received the drug product ["Open label" subject, (OL)]. Baseline vascular mapping (cephalic vein ≥2.5 mm; artery ≥2 mm; vein depth ≤5 mm) was performed to ensure suitability.

Results

There were no product related serious adverse events. Table lists key demographic and outcome metrics. Time to First Dialysis (TTFD): Time from AVF creation, to the time when the fistula can support three consecutive 2 needle dialysis sessions with a mean dialysis pump flow of ≥300 mL/min (2N/300). Fistula Suitability for Dialysis at 6 months (FSD6): Ability to use the fistula (2N/300) for two thirds of the dialysis sessions during a 30 day suitability ascertainment period commencing on day 150.

Excluding the 2 AVF that thrombosed early, TTFD was <90 days for 11/16 (69%) subjects.

Conclusion

1. Time to maturation and AVF suitability for dialysis at 6 months in the open label Phase 3 subjects are similar to Phase 2 results and signal an improvement in comparison to historical controls.
2. Results are promising and may suggest that prophylactic local treatment with sirolimus at time of AVF creation could *predictably* reduce catheter dependence to less than 90 days with durable AV fistula functionality.

Enrollment is ongoing in the ACCESS trial.

Phase	N	Age (y) Mean (range)	Male	Diabetes	RCF	BCF	Thrombosis*	TTFD (d) Median (range)**	FSD6
Phase 2	30	51 (25-77)	60%	20%	22	8	13% (4/30)	42 (27-150)	76%
Phase 3 (OL)	18	61 (38-91)	89%	61%	10	8	11% (2/18)	64 (38-137)	89%

* Within 2 weeks of surgery ** Excludes thrombosis prior to first cannulation

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