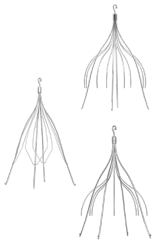
Final Results of a Prospective Multicenter Study of the Günther Tulip and Celect IVC Filters

Rabih Chaer, MD, MSC.
on behalf of the study investigators
Professor and Chief,
UPMC Division of Vascular Surgery



UPMC LIFE CHANGING MEDICINE

Disclosures

I was a coinvestigator on the CIVC trial
I have no relevant financial disclosures for this talk

Study Objective and Design

- **Purpose:** To further evaluate the safety and effectiveness of Cook's commercially available IVC filters (Günther Tulip filter and Celect filters) in patients in need of temporary or permanent IVC filter placement for the prevention of pulmonary embolism (PE)
- **Design**: Prospective, multicenter, single-arm, IDE study
- **Sample Size**: 320 patients with Celect filters (i.e., Celect Platinum Vena Cava Filter or Celect Vena Cava Filter) and up to 150 patients with Günther Tulip filters
- **Follow-up**: for 2 years or 30 days after filter retrieval
- **Primary Effectiveness Endpoint**: Rate of technical placement success and 12-month freedom from new symptomatic PE while a filter is indwelling
- **Primary Safety Endpoint**: Rate of 12-month freedom from MAEs (clinical perforation, clinical migration, clinical fracture, embolization of the filter or filter fragments to the heart or lungs, IVC thrombotic occlusion, new symptomatic DVT while the filter is indwelling, access site complications with clinical sequelae, procedure-/device-related death)

Enrollment Criteria

Inclusion Criterion

- Patients ≥18 years may be suitable for inclusion in the study if he/she requires temporary or permanent IVC filter placement for the prevention of PE

Notable Exclusion Criteria

- At risk of septic embolism
- Life expectancy less than 12 months
- Existing IVC filter
- Duplicate IVC
- Anatomy that would prevent safe filter placement (e.g., condition of access vessels)
- IVC diameter > 30 mm or < 15 mm
- Pregnant or planning to become pregnant in the next 12 months

Baseline Patient Demographics

- 473 patients enrolled at 28 sites (US, UK, AUS) between 2014 and 2017
- 324 Celect and 149 Günther Tulip
- Mean age 61.1 ± 16.1 years
- 57.3% male

Demographic	Mean ± SD (Min-Max) or Percent Patients (number/total number)		
	Celect Stratum (N=324)	Günther Tulip Stratum (N=149)	Total (N=473)
Age (years; mean ± SD (range))	60.7 ± 16.4 (18 – 94)	61.9 ± 15.4 (20 – 92)	61.1 ± 16.1 (18 – 94)
Gender, % (n)			
Male	56.8% (184)	58.4% (87)	57.3% (271)
Female	43.2% (140)	41.6% (62)	42.7% (202)

Baseline Patient Medical History

- Patient characteristics were similar between the two strata
- History of VTE or current DVT was common:
  - Previous DVT (34%)
  - Current DVT (61.6%)
  - Previous PE (24.3%)
  - Current PE (29.8%)

Medical condition	Mean ± SD (Min-Max) or Percent Patients (number/total number)		
	Celect Stratum (N=324)	Günther Tulip Stratum (N=149)	Total (N=473)
Previous DVT (history of DVT)	32.7% (106)	36.9% (55)	34.0% (161)
Current DVT (per site baseline assessment)	64.4% (199/309)	55.6% (80/144)	61.6% (279/453)
Previous PE	24.4% (79)	24.2% (36)	24.3% (115)
Current PE (per site baseline assessment)	28.4% (92)	32.9% (49)	29.8% (141)
Bleeding diathesis or coagulopathy	9.3% (30)	14.1% (21)	10.8% (51)
Cancer (history of/current)	33.6% (109)	43.6% (65)	36.8% (174)
Current cancer	64.2% (70)	73.8% (48)	67.8% (118/174)
Chemotherapy in past 12 mos	33.0% (36)	35.4% (23)	33.9% (59/174)

DVT=Deep vein thrombosis; PE=pulmonary embolism; VTE=venous thromboembolism

Indications for Filter Placement

- Most filters placed as temporary devices (94.9%)
- Indication for filter placement:
  - Current DVT (48.4%) and/or Current PE (20.7%)
  - No VTE; considered at risk (30.9%)

Indication Details[a]	Celect Stratum (N=324)	Günther Tulip Stratum (N=149)	Total (N=473)
Current DVT	50.0% (162)	45.0% (67)	48.4% (229)
Current PE	19.1% (62)	24.2% (36)	20.7% (98)
Complication to anticoagulation	4.9% (16)	4.7% (7)	4.9% (23)
Contraindication to anticoagulation	37.3% (121)	47.0% (70)	40.4% (191)
Failure of anticoagulation	1.9% (6)	0.7% (1)	1.5% (7)
No contraindication to anticoagulation, but added risk	23.5% (76)	16.8% (25)	21.4% (101)
Poor compliance with anticoagulation	1.2% (4)	0% (0)	0.8% (4)
No VTE; considered at risk:	30.9% (100)	30.9% (46)	30.9% (146)
History of prior VTE	13.6% (44)	17.4% (26)	14.8% (70)
Hypercoagulable	3.7% (12)	6.0% (9)	4.4% (21)
Recent Trauma	10.5% (34)	3.4% (5)	8.2% (39)
Surgery	18.5% (60)	26.2% (39)	20.9% (99)
Other medical condition	2.5% (8)[b]	4.7% (7)[c]	3.2% (15)
Contraindication to anticoagulation	15.4% (50)	20.1% (30)	16.9% (80)

[a]Subject could have more than one indication for filter placement.
[b]Bleeding on anticoagulation (1), history of PE/DVT (5), immobilized in bed (1), metastatic cancer (1), family history of DVT/PE (1), previous massive PE (1), and profound anemia (2).
[c]Cancer (5), previous DVT (1), myelofibrosis (1), prolonged immobilization (2), rectus sheath hematoma (1), and renal cell carcinoma (1).

Excellent Effectiveness Outcomes

- Technical placement success and 12-mo freedom from new symptomatic PE for the **Celect Stratum (97.8%)** met the predefined performance goal (90%)
- Secondary outcomes for the **Günther Tulip stratum (98.7%)** (without hypothesis testing) were also positive

Measure	Stratum	Endpoint	Rate (n/N)	95% CI	PG
Technical placement success and 12-month freedom from new symptomatic PE while a filter is indwelling[a]	Celect Stratum	Primary Endpoint	97.8% (317/324)[b]	(95.6%, 99.1%)	90%
	Gunther Tulip Stratum	Secondary Endpoint	98.7% (147/149)	-	-
	Total Population	Secondary Endpoint	98.1% (464/473)	-	-

[a]The Exact binomial test model was used for analyses. The denominators are the number of subjects evaluable for the endpoint.
[b]4 technical failures and 3 new symptomatic PEs
CI=Confidence Interval; PG=Performance Goal

Favorable Safety Outcomes

- KM estimates for freedom from events support filter safety and effectiveness
  - One fracture occurred during a filter retrieval procedure (with use of GTRS, loop snare technique, and forceps); a filter strut embolized to the right ventricle.
  - One device-related death with 30 days of placement was attributed to Phlegmasia cerulea dolens.
  - Clinical perforation was an imaging outcome in 50 total patients and was associated with clinical symptoms in one patient (abdominal pain).

Endpoint (Freedom from event)	Kaplan-Meier Estimate (Number of patients at risk, Number of events)				
	3 mos	6 mos	12 mos	18 mos	24 mos
New symptomatic PE while a filter is indwelling	99.5% (360, 2)	99.1% (187, 3)	98.5% (96, 4)	98.5% (60, 4)	98.5% (26, 4)
Clinical perforation	98.4% (358, 7)	97.2% (186, 11)	89.1% (90, 20)	60.5% (38, 45)	50.1% (16, 49[a])
Filter embolization	100% (362, 0)	100% (189, 0)	100% (98, 0)	100% (62, 0)	100% (28, 0)
IVC thrombotic occlusion	99.1% (360, 4)	98.8% (186, 5)	97.5% (94, 7)	97.5% (60, 7)	97.5% (27, 7)
New symptomatic DVT	96.5% (350, 15)	93.8% (174, 22)	93.2% (89, 23)	89.4% (54, 26)	89.4% (23, 26)
Procedure or device related death	99.8% (362, 1)	99.8% (189, 1)	99.8% (98, 1)	99.8% (62, 1)	99.8% (28, 1)
Access site complications with clinical sequelae	100% (362, 0)	100% (189, 0)	100% (98, 0)	100% (62, 0)	100% (28, 0)
Filter fracture	100% (362, 0)	100% (189, 0)	100% (98, 0)	98.9% (61, 1)	98.9% (27, 1)
Filter migration >20mm	100% (358, 0)	100% (186, 0)	99.0% (95, 1)	98.0% (58, 2)	98.0% (26, 2[b])

[a]One clinical perforation occurred after 24 mos; total of 50 events in the study.
[b]Caudal movement of a Celect and Gunther Tulip IVC filter ≥20 mm was observed on 12-month follow-up imaging, without clinical sequelae.

Favorable Safety Outcomes

- Primary Safety for Celect stratum:
  - Protocol-defined Kaplan-Meier estimate for 12-month freedom from MAE (81.5%) did not meet the performance goal (80%). 204 patients were censored due to a successful retrieval without a safety event, making the 12-month estimate less precise
  - The FDA agreed upon post-hoc analysis considered a successful retrieval in absence of MAE a success (in line with clinical practice); in this analysis the rate (86.7%) met the performance goal (80%)
- Secondary endpoint for Günther Tulip stratum was favorable (90.6%)

Measure	Stratum	Endpoint	Rate (No. at risk, No. of events or n/N)	95% CI	PG
12-month freedom from MAE[a]	Celect Stratum	Primary Endpoint	81.5% (57, 32)	(72.6%, 90.4%)	80%
Post-hoc: 12-month freedom from MAE[b]			86.7% (281/324)	(82.5%, 90.2%)	
12-month freedom from MAE	Günther Tulip Stratum	Secondary Endpoint	90.6% (135/149)	-	-
	Total Population	Secondary Endpoint	87.9% (416/473)	-	-

[a]The Z-statistic was used for analyses, with Kaplan-Meier estimate for freedom from major adverse events. [b]The Exact binomial test model was used for analyses. The denominators are the number of subjects evaluable for the endpoint.
CI=Confidence Interval; PG=Performance Goal

High Filter Retrieval Success

- Filter retrieval attempted in 70.8% of patients (335/473)
- Successful retrieval rate: 94.9% (318/335)
- Failed retrievals in **15 patients** (17 attempts):
  - Hook embedded in the vessel (**n=11**)
  - Hook oriented towards the vessel wall (**n=9**)
  - Excessive growth at the filter legs (**n=2**)
  - Ingrowth of intima into struts, unable to reach filter hook with snare, hook oriented towards the vessel wall and patient intolerant of procedure (**n=3**)
- 3 patients with initially unsuccessful filter retrieval attempts later underwent successful retrievals

Filter Retrieval Information	Reported		
	Celect Stratum	Günther Tulip Stratum	Total
Successful filter retrieval attempts	95.2% (219/230)	94.3% (99/105)	94.9% (318/335)
Days to successful filter retrieval (mean ± SD (N, min-max))	134.0 ± 111.4 (219, 0 – 603)	120.2 ± 101.8 (99, 0 – 594)	129.7 ± 108.5 (318, 0 – 603)
Unsuccessful filter retrieval attempts	4.8% (11)	5.7% (6)	5.1% (17)

Conclusion

- The CIVC study demonstrated excellent safety and effectiveness outcomes for the Celect filters and the Günther Tulip filter
  - High rate of filter retrieval attempts and rate of successful filter retrievals
  - Low rate of new symptomatic PE, symptomatic clinical perforation, filter fracture, filter migration, and filter embolization
- The CIVC study was conducted at the same time as the PRESERVE study; results from both studies are consistent with previously reported rates for filter complications (e.g., filter embolization, clinically significant perforation, new DVT, IVC thrombotic occlusion)