## Appendix Table 5. Features of Patent Foramen Ovale Closure Device Trials.

| Trial | Year of Publication | Enrollment/ Follow-up | Geography | Type of Device | Inclusion Criteria | | | Patient Number | Follow-Up Years (mean)/ Patient-years | Ratio of Follow-Up Dev/Med[a] |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | Event Type | Timing | Age | | | |
| CLOSURE | 2012 | E: 2003-2008<br>F: 2003-2010 | United States, Canada | STARflex (NMT Medical) | Cryptogenic IS or TIA | < 6 mo | 18-60 | 909 | 1.7/1555 | 1.06 |
| PC Trial | 2013 | E: 2003-2009<br>F: 2000-2012 | Europe, Canada, Brazil, Australia | Amplatzer | Cryptogenic IS or periph embolism | No restriction | <60 | 414 | 4.1/1681 | 1.04 |
| RESPECT | 2013/2017 | E: 2003-2011<br>F: 2003-2016 | United States, Canada | Amplatzer | Cryptogenic IS (Tissue-Def) | < 9 mo | 18-60 | 980 | 5.8/5688 | 1.14 |
| CLOSE | 2017 | E: 2007-2014<br>F: 2007-2016 | France, Germany | Multiple[d] | Cryptogenic IS (Tissue-Def) | < 6 mo | 16-60 | 473 (653)[b] | 5.3/2507 | 1.04 |
| REDUCE | 2017 | E: 2008-2015<br>F: 2008-2016 | Europe, Canada, United States | Helex or Cardioform (Gore) | Cryptogenic IS (Tissue-Def) | < 6 mo | 18-59 | 664 | 3.4/2232 | 1.10 |
| DEFENSE-PFO | 2018 | E: 2011-2017<br>F: 2011-2017 | South Korea | Amplatzer | Cryptogenic IS (Tissue-Def) | < 6 mo | 18-80 | 120 | 1.6[c]/≈187 | 1.03 |

[a]Mean duration of follow-up among device patients/mean duration of follow-up among medical patients. Longer follow-up among device patients occurred because of (1) more end point events in medical patients, ending study participation, and (2) more dropouts in medical patients, in part to pursue device placement outside of the trials.
[b]Full results reported for 473 patients randomized to closure and medical antiplatelet therapy groups, pending for 180 randomized to the medical anticoagulation therapy group.
[c]For DEFENSE-PFO, only follow-up years estimated from the Kaplan–Meier curve of the fully-reported time period—the first 2 years after enrollment.
[d]Devices included Amplatzer PFO occluder (121), Intrasept PFO occluder (31), Premere (22), Starflex septal occluder system (21), Amplatzer cribriform occluder (15), Figulla Flex II PFO occluder (15), Atriasept II occluder (3), Amplatzer ASD occluder (2), Figulla Flex II UNI occluder (2), Gore septal occluder (2), Figulla Flex II ASD occluder (1).
CLOSE indicates Patent Foramen Ovale Closure or Anticoagulants Versus Antiplatelet Therapy to Prevent Stroke Recurrence; CLOSURE, Evaluation of the STARFlex Septal Closure System in Patients With a Stroke and/or Transient Ischemic Attack due to Presumed Paradoxical Embolism Through a Patent Foramen Ovale; DEFENSE-PFO, Device Closure Versus Medical Therapy for Cryptogenic Stroke Patients With High-Risk Patent Foramen Ovale; IS, ischemic stroke; PC Trial, Clinical Trial Comparing Percutaneous Closure of Patent Foramen Ovale Using the Amplatzer PFO Occluder With Medical Treatment in Patients With Cryptogenic Embolism; REDUCE, Gore REDUCE Clinical Study; RESPECT, Randomized Evaluation of Recurrent Stroke Comparing PFO Closure to Established Current Standard of Care Treatment; and TIA, transient ischemic attack.