

# Important Clinical Trials in Stroke

| Study   | Year | Questions?   | Answers:   |
|---|------|--|--|
| <b>Stroke prophylaxis:</b>  |      |  |  |
| <b>RAF</b><br>Early stroke recurrence and cerebral bleeding in patients with AF and acute ischemic stroke treated with anticoagulants for secondary prevention                        | 2015 | When to start anticoagulation after AIS in patients with AF?<br><br>How to restart anticoagulation after AIS in patients with AF?      | Within 4-14 days of onset was associated with lowest combined risk of ischemia and hemorrhage<br><br>Warfarin alone without heparin bridge was associated with lowest risk |
| <b>BRIDGE</b><br>(Warfarin held 5 days before surgery, LMWH started 3 days and stopped 1 day before surgery, Warfarin and LMWH (till INR reached 2) were restarted 12h after surgery) | 2015 | Should we bridge with LMWH while stopping warfarin before surgery in patients with AF?   | Don't bridge with LMWH before surgery in patients with AF  |
| <b>ARCH</b>   | 2014 | ASA + clopidogrel vs Warfarin in aortic arch plaque > 4mm?   | Study not completed due to lack of funds   |
| <b>CHANCE</b>   | 2013 | Is it beneficial to combine ASA and clopidogrel for 21 days after acute stroke?  | Beneficial: reduced risk with no increase in bleeding  |
| Antiplatelet treatment for prevention of CVA in patients with vascular disease.   | 2013 | Is it beneficial to combine clopidogrel & aspirin for primary and secondary stroke prevention in patients with cardiovascular disease? | Beneficial: DAPS (ASA + Clopidogrel) was superior (RR reduction 20%) compared with ASA alone in stroke prevention with no increase in ICH.                                 |
| <b>CADISS-NR</b>  | 2012 | Antiplatelet Vs Anticoagulation for dissection?  | No significant difference<br><b>Cons:</b> Underpowered – non-randomized study  |
| <b>WARCEF</b>   | 2012 | Should we use aspirin or warfarin for primary stroke prevention in patients with low EF in sinus rhythm?                               | No significant difference  |
| <b>ARISTOTLE</b>  | 2011 | Apixaban Vs Warfarin in patients with Afib (CHADS $\geq$ 1)?   | Apixaban is superior with less risk of bleeding  |
| <b>AVERROS</b>  | 2011 | Apixaban Vs Aspirin in patients with afib (CHADS $\geq$ 1) who are unsuitable for warfarin?  | Apixaban is superior   |
| <b>ROCKET-AF</b>  | 2011 | Rivaroxaban VS Warfarin in Afib?   | Rivaroxaban is non-inferior to warfarin<br>Rivaroxaban is associated with less ICH but more GI bleeding risk.  |
| <b>CLAIR</b>  | 2011 | Clopidogrel + ASA Vs ASA alone for patients with acute symptomatic cerebral or carotid stenosis?                                       | ASA 160:750 + Plavix load 300 then maintenance is superior   |

|   |      |   |  |
|---|------|---|--|
| <b>SPS-3</b>  | 2011 | Clopidogrel + ASA Vs ASA alone for patients with acute lacunar stroke?  | ASA 325mg was better than DAP  |
| <b>EARLY</b>  | 2010 | Dipyridamole 200mg bid + ASA 25 versus aspirin alone for secondary stroke prevention within 24h of onset?   | Dipyridamole 200mg bid + ASA 25 bid is not superior to ASA monotherapy   |
| <b>Stroke Acute management:</b>                                       |      |   |  |
| <b>PASS</b>   | 2015 | Does prophylactic ceftriaxone in AIS patients improve outcome?  | No   |
| <b>CATIS</b><br>China Antihypertensive Trial in Acute Ischemic Stroke | 2014 | BP control (<140/90) Vs permissive HTN in acute ischemic stroke?  | No beneficial effect of reducing BP (<140) in AIS  |
| <b>ReCLAIM I</b>  | 2014 | Is intravascular cooling in acute ischemic stroke patients with poor outcomes protective against reperfusion hemorrhage after endovascular therapy? | Hypothermia was protective against ICH after intravascular thrombectomy  |
| <b>DESTINY II</b>   | 2014 | Hemicraniectomy in patients >60 years with malignant MCA infarction?  | Hemicraniectomy within 48h is associated with more survival (57% vs 28%), less severe disability (38% vs 18%) and less herniation. |
| <b>CLEAR ER</b>   | 2013 | Is it beneficial to add eptifibatide to IV tPA?   | No significant difference  |
| <b>ALIAS</b>  | 2013 | Does high dose albumin improve outcome in AIS?  | No   |
| <b>DEFUSE 2</b>   | 2012 | Does selecting patients with diffusion/perfusion mismatch for intervention affect the net outcome?  | Yes<br>OR for favorable outcome was 8.8 in patients with mismatch and only 0.2 in patients without mismatch                        |
| <b>FLAME</b>  | 2012 | Does Fluoxetine improve motor recovery after acute ischemic stroke?   | Yes (FMM score 12.4 vs 2.1)  |
| <b>EAGLE</b>  | 2010 | IA tPA Vs conservative treatment in patients with CRAO?   | IA tPA was not superior  |
| <b>Modifying Risk Factors:</b>  |      |   |  |
| <b>Intracranial stenosis:</b>   |      |   |  |
| <b>VISSIT</b>   | 2015 | Does balloon expandable stenting help patients with symptomatic intracranial stenosis?  | Balloon stenting was harmful   |
| <b>COSS</b>   | 2011 | Does extracranial-Intracranial arterial bypass surgery help in stroke prevention in patient ICA occlusion?  | No   |
| <b>SAMMPRIS</b>   | 2011 | Stenting + medical therapy Vs medical therapy alone for stroke prevention in patients with intracranial arterial stenosis >70%                      | Stenting was harmful<br>ASA 325 indefinite + Plavix for 3 months + SBP < 140, LDL < 70 was more helpful                            |
| <b>Atrial fibrillation:</b>   |      |   |  |

|                           |      |  |  |
|---------------------------|------|--|--|
| <b>PROTECT AF</b>         | 2013 | Comparing Watchman percutaneous Lt atrial appendage closure device to Warfarin in patients with AF over 2 years. (Watchman device placed followed by 45 days of warfarin then 4.5 months of dual antiplatelet then ASA lifelong) | Watchman device is not inferior to warfarin<br><b>Cons:</b> Non blinded – manufacturer sponsored trail   |
| <b>PFO</b>                |      |  |  |
| <b>RESPECT</b>            | 2013 | Does the closure of PFO after cryptogenic stroke helps in secondary stroke prevention?   | PFO closure is not superior to medical therapy but associated with more adverse outcomes after surgery.  |
| <b>CLOSURE I</b>          | 2012 | Does the closure of PFO after cryptogenic stroke helps in secondary stroke prevention?   | PFO closure with Starflex is not superior to medical therapy but associated with post procedural Afib  |
| <b>ICA stenosis</b>       |      |  |  |
| <b>CREST</b>              | 2010 | CAS Vs CAE for treatment of carotid artery stenosis  | CAS associated with more periprocedural risk of stroke<br>CEA associated with more periprocedural MI<br><b>Patients &gt; 70 years had better outcome with CEA</b><br><b>Patients &lt; 70 years had better outcome with CAS</b> |
| <b>Cryptogenic stroke</b> |      |  |  |
| <b>EMBRACE</b>            | 2014 | Noninvasive 30 day cardiac monitoring vs 24h monitoring in detecting afib in patients with cryptogenic stroke > 55 years.  | Afib detected in 16.1% of active group vs 3.7% in controls<br>75% of patients who were found to have afib were captured during first 2 weeks.  |
| <b>Crystal AF</b>         | 2014 | Insertable cardiac monitoring vs conventional follow up in detecting afib in patients with cryptogenic stroke  | Afib detected in 8.9% of active group vs 1.4% in controls at 6 months, increased to 12.4% of active group vs 2% in controls at 12 months   |

DAP: dual antiplatelet therapy (aspirin + Clopidogrel)