## Supplemental tables

## Supplemental table 1. Participation centers

| Department  | Hospital  | City          | Province          | Site PI               |
|---|---|---------------|-------------------|-----------------------|
| Department of<br>Interventional<br>Neuroradiology | Beijing Tiantan Hospital,<br>Capital Medical University                           | Beijing       | Beijing           | Zhongrong Miao        |
| Department of Emergency                           | Xiangtan Central Hospital   | Xiangtan      | Hunan             | Guangxiong<br>Yuan    |
| Department of<br>Neurology                        | Linyi People's Hospital   | Linyi         | Shandong          | Hongxing Han          |
| Department of<br>Neurology                        | Zhangzhou Affiliated Hospital of Fujian Medical University                        | Zhangzho<br>u | Fujian            | Wenhuo Chen           |
| Department of<br>Neurosurgery                     | Tianjin huanhu hospital   | Tianjin       | Tianjin           | Ming Wei              |
| Department of Neurology                           | Anyang People's Hospital  | Anyang        | Henan             | Jiangang Zhang        |
| Department of Neurology                           | Yijishan Hospital of Wannan<br>Medical College                                    | Wuhu          | Anhui             | Zhiming Zhou          |
| Department of Neurology                           | The first people's hospital of Chenzhou   | Chenzhou      | Hunan             | Xiaoxi Yao            |
| Department of Neurology                           | Bin zhou People's Hospital  | Binzhou       | Shandong          | Guoqing Wang          |
| Department of Neurology                           | Yancheng Third People's<br>Hospital   | Yancheng      | Jiangsu           | Weigen Song           |
| Department of<br>Neurology                        | Lishui Municipal Central<br>Hospital  | Lishui        | Zhejiang          | Xueli Cai             |
| Department of<br>Neurology                        | China-Japan Union Hospital of Jilin University                                    | Changchu<br>n | Jinlin            | Guangxian Nan         |
| Department of<br>Neurointervention                | Dalian Municipal Central<br>Hospital affiliated with Dalian<br>Medical University | Dalian        | Liaoning          | Di Li                 |
| Department of<br>Neurosurgery                     | Guangdong Provincial Hospital of Chinese Medicine                                 | Guangzho<br>u | Guangdon<br>g     | Alvin Yi-Chou<br>Wang |
| Department of<br>Neurology                        | ZhongShan City People's<br>Hospital   | Guangzho<br>u | Guangdon<br>g     | Wentong Ling          |
| Department of<br>Neurology                        | Shantou Central Hospital  | Shantou       | Guangdon<br>g     | Chuwei Cai            |
| Department of<br>Neurology                        | Nanyang Central Hospital  | Nanyang       | Henan             | Changming Wen         |
| Department of Neurology                           | Taizhou hospital of Zhejiang<br>Province  | Taizhou       | Zhejiang          | En Wang               |
| Department of Neurosurgery                        | Liaocheng People's Hospital   | Liaocheng     | Shandong          | Liyong Zhang          |
| Department of<br>Neurology                        | Baotou Centre Hospital  | Baotou        | Inner<br>Mongolia | Changchun Jiang       |
| Department of<br>Neurology                        | Shenzhen Hospital, Southern<br>Medical University                                 | Shenzhen      | Guangdon          | Yajie Liu             |
| Department of<br>Neurology                        | Maoming People's Hospital   | Maoming       | Guangdon          | Geng Liao             |
| Department of<br>Neurology                        | The Second Affiliated Hospital of GuangZhou Medical University                    | Guangzho<br>u | Guangdon<br>g     | Xiaohui Chen          |

| Department of    | Henan Provincial People's        | Zhengzho  | Henan     | Tianxiao Li    |
|------------------|----------------------------------|-----------|-----------|----------------|
| Cerebrovascular  | Hospital, Zhengzhou University   | u         | Tichan    | Tiunxiuo Ei    |
| Disease          | Trospital, Zhengzhoù emversity   |           |           |                |
| Department of    | Yongchuan Hospital of            | Chongqing | Chongqin  | Shudong Liu    |
| Neurology        | Chongqing Medical University     | changqing | g         | Shadong Liu    |
| Department of    | The affiliated hospital of South | Luzhou    | Sichuan   | Jinglun Li     |
| Neurology        | West medical university          | Luziiou   | Sichaan   | omgran Er      |
| Department of    | Shanxi Provincial People's       | Taiyuan   | Shanxi    | Yaxuan Sun     |
| Neurology        | Hospital                         | Taryaan   | Shanxi    | T dAddit Sun   |
| Department of    | The Second Affiliated Hospital   | Xiamen    | Fujian    | Na Xu          |
| Neurology        | to Xiamen Medical College        | Zuminen   | 1 ujiun   | 114 214        |
| Department of    | Shengli Oilfield Central         | Dongying  | Shandong  | Zong'en Gao    |
| Neurology        | Hospital                         | Dongying  | Shandong  | Zong en ouo    |
| Department of    | Songyuan Jilin oil Field         | Songyuan  | Jilin     | Dongsheng Ju   |
| Neurology        | Hospital                         | Bongyuun  | 31111     | Dongsheng va   |
| Department of    | Liao Cheng the third people's    | Liaocheng | Shandong  | Cunfeng Song   |
| Interventional   | hospital                         | Lidocheng | Shandong  | Cumeng bong    |
| Neuroradiology   | позриш                           |           |           |                |
| Department of    | The First People's Hospital of   | Changzho  | Jiangsu   | Jinggang Xuan  |
| Neurology        | Changzhou                        | u         | Jangsu    | Jinggang Adan  |
| Department of    | Taiyuan Central Hospital         | Taiyuan   | Shanxi    | Feng Zhou      |
| Neurology        | Taryuan Centrai Hospitai         | Taryuan   | Shanxi    | Teng Zhou      |
| Department of    | Affiliated Jiangmen Traditional  | Jiangmen  | Guangdon  | Qing Shi       |
| Neurology        | Chinese Medicine Hospital of     | Jungmen   | g         | Qing oin       |
| rediology        | Ji'nan University                |           | 5         |                |
| Department of    | Sichuan Mianyang 404 Hospital    | Mianyang  | Sichuan   | Jun Luo        |
| Neurology        | Sienaan Waanyang 10 1 1105pian   | Wilding   | Siendan   | Juli Euo       |
| Department of    | JingJiang People's Hospital, the | Jingjiang | Jiangsu   | Yan Liu        |
| Neurology        | Seventh Affiliated Hospital of   | Jingjiang | Jangsu    | Tan Era        |
| reardings        | Yangzhou University              |           |           |                |
| Department of    | Tianjin TEDA Hospital            | Tianjin   | Tianjin   | Zaiyu Guo      |
| Neurosurgery     | Trangin 122/11/05prair           | 1 miljin  | 1 miljiii | Zuryu Guo      |
| Department of    | The second Nanning People's      | Nanning   | Guangxi   | Tong Li        |
| Neurosurgery     | Hospital                         | 1 tunning | Guangai   | Tong Er        |
| Department of    | West China Hospital, Sichuan     | Chengdu   | Sichuan   | Hongbo Zheng   |
| Neurology        | University                       | Chengua   | Sicildan  | Trongoo Zateng |
| Department of    | First Affiliated Hospital School | Shihezi   | Xinjiang  | Linzhi Dai     |
| Neurosurgery     | of Medicine Shihezi University   |           | Tinjiang  | Zinzin z ui    |
| Department of    | Siping Central People's Hospital | Siping    | Jilin     | Junfeng Zhao   |
| Neurology        |                                  | 2-1-1-8   |           |                |
| Emergency and    | Langfang Changzheng Hospital     | Langfang  | Hebei     | Liqiang Gui    |
| Critical Stroke  |                                  |           |           |                |
| Ambulance Center |                                  |           |           |                |
| Department of    | Beijing Luhe Hospital, Capital   | Beijing   | Beijing   | Xiaokun Geng   |
| Neurology        | Medical University               |           | ,,        |                |
| Department of    | Mianyang Central Hospital        | Mianyang  | Sichuan   | Yufeng Tang    |
| Neurology        |                                  | ,         | .,        |                |
| Department of    | Hangzhou First People's          | Hangzhou  | Zhejiang  | Congguo Yin    |
| Neurology        | Hospital                         | 2         |           |                |
| Department of    | The affiliated Hospital of       | Guiyang   | Guizhou   | Hua Yang       |
| Neurosurgery     | -                                |           |           |                |
| 1.carobargery    | Calling integretal Chirototty    | 1         | ı         | 1              |

Supplemental table 2. Study organization

| Department   |  |  |  |  |  |
|--|--|--|--|--|--|
| 2 opur unom  | Hospital   |  |  |  |  |
|  |  |  |  |  |  |
| Department of Neurology                            | Beijing Tiantan Hospital, Capital Medical University   |  |  |  |  |
| Department of Neurology                            | Beijing Tiantan Hospital, Capital Medical<br>University  |  |  |  |  |
| Department of Neurology                            | Beijing Tiantan Hospital, Capital Medical University   |  |  |  |  |
| Department of Neurology                            | University of California at Los Angeles  |  |  |  |  |
| Department of Interventional<br>Neuroradiology     | Beijing Tiantan Hospital, Capital Medical University   |  |  |  |  |
| Department of Neurosurgery                         | The Affiliated Hospital of Guizhou Medical University  |  |  |  |  |
| Department of Neurosurgery,<br>Division of Surgery | St Michael's Hospital, University of Toronto   |  |  |  |  |
| g Core Lab   |  |  |  |  |  |
| Tiantan Neuroimaging Center of Excellence (T-NICE) | China National Clinical Research Center for<br>Neurological Diseases   |  |  |  |  |
| Tiantan Neuroimaging Center of Excellence (T-NICE) | China National Clinical Research Center for<br>Neurological Diseases   |  |  |  |  |
| Tiantan Neuroimaging Center of Excellence (T-NICE) | China National Clinical Research Center for<br>Neurological Diseases   |  |  |  |  |
| Department of Neurology                            | Qilu Hospital, Shandong University   |  |  |  |  |
| itoring board                                      |  |  |  |  |  |
| Neurovascular Center                               | Changhai Hospital, Naval Medical University  |  |  |  |  |
| Department of Medical<br>Statistics                | Peking University First Hospital   |  |  |  |  |
| Department of Neurology                            | The Southwest Hospital of Army Medical University  |  |  |  |  |
| ittee  |  |  |  |  |  |
| Department of Neurology                            | Huashan Hospital, Fudan University   |  |  |  |  |
| Department of Neurology                            | The First Affiliated Hospital of Zhengzhou University  |  |  |  |  |
| Department of Neurology                            | Huashan Hospital, Fudan University   |  |  |  |  |
|  |  |  |  |  |  |
| Department of Interventional<br>Neuroradiology     | Beijing Tiantan Hospital, Capital Medical University   |  |  |  |  |
|  | Department of Neurology  Department of Neurology  Department of Interventional Neuroradiology  Department of Neurosurgery  Department of Neurosurgery, Division of Surgery  Genter of Excellence (T-NICE)  Tiantan Neuroimaging Center of Excellence (T-NICE)  Tiantan Neuroimaging Center of Excellence (T-NICE)  Department of Neurology  Itoring board  Neurovascular Center  Department of Medical Statistics  Department of Neurology  Ittee  Department of Neurology  Department of Neurology |  |  |  |  |

| Xiaochuan Huo   | Department of Interventional<br>Neuroradiology | Beijing Tiantan Hospital, Capital Medical University                        |  |  |  |  |
|-----------------|--|---|--|--|--|--|
| Gaoting Ma      | Department of Interventional<br>Neuroradiology | Beijing Tiantan Hospital, Capital Medical University                        |  |  |  |  |
| Guangxiong Yuan | Department of Emergency                        | Xiangtan Central Hospital   |  |  |  |  |
| Hongxing Han    | Department of Neurology                        | Linyi People's Hospital   |  |  |  |  |
| Wenhuo Chen     | Department of Neurology                        | Zhangzhou Affiliated Hospital of Fujian<br>Medical University               |  |  |  |  |
| Ming Wei        | Department of Neurosurgery                     | Tianjin huanhu hospital   |  |  |  |  |
| Jiangang Zhang  | Department of Neurology                        | Anyang People's Hospital  |  |  |  |  |
| Zhiming Zhou    | Department of Neurology                        | Yijishan Hospital of Wannan Medical College                                 |  |  |  |  |
| Xiaoxi Yao      | Department of Neurology                        | Chenzhou First One Hospital   |  |  |  |  |
| Guoqing Wang    | Department of Neurology                        | Bin zhou People's Hospital  |  |  |  |  |
| Weigen Song     | Department of Neurology                        | Yancheng Third People's Hospital  |  |  |  |  |
| Xueli Cai       | Department of Neurology                        | Lishui Municipal Central Hospital   |  |  |  |  |
| Guangxian Nan   | Department of Neurology                        | China-Japan Union Hospital of Jilin University                              |  |  |  |  |
| Di Li           | Department of<br>Neurointervention             | Dalian Municipal Central Hospital affiliated with Dalian Medical University |  |  |  |  |
| Yizhou Wang     | Department of Neurosurgery                     | Guangdong Provincial Hospital of Chinese<br>Medicine                        |  |  |  |  |
| Wentong Ling    | Department of Neurology                        | ZhongShan City People's Hospital  |  |  |  |  |
| Chuwei Cai      | Department of Neurology                        | Shantou Central Hospital  |  |  |  |  |
| Changming Wen   | Department of Neurology                        | Nanyang Central Hospital  |  |  |  |  |
| En Wang         | Department of Neurology                        | Taizhou hospital of Zhejiang Province                                       |  |  |  |  |
| Liyong Zhang    | Department of Neurosurgery                     | Liaocheng People's Hospital   |  |  |  |  |
| Changchun Jiang | Department of Neurology                        | Baotou Centre Hospital  |  |  |  |  |
| Yajie Liu       | Department of Neurology                        | Shenzhen Hospital, Southern Medical<br>University                           |  |  |  |  |
| Geng Liao       | Department of Neurology                        | Maoming People's Hospital   |  |  |  |  |
| Xiaohui Chen    | Department of Neurology                        | The Second Affiliated Hospital of GuangZhou Medical University              |  |  |  |  |
| Tianxiao Li     | Department of<br>Cerebrovascular Disease       | Henan Provincial People's Hospital, Zhengzhou<br>University                 |  |  |  |  |
| Shudong Liu     | Department of Neurology                        | Yongchuan Hospital of Chongqing Medical<br>University                       |  |  |  |  |
| Jinglun Li      | Department of Neurology                        | The affiliated hospital of South West medical                               |  |  |  |  |

|               |   | university   |
|---------------|---|--|
| Yaxuan Sun    | Department of Neurology                           | Shanxi Provincial People's Hospital  |
| Na Xu         | Department of Neurology                           | The Second Affiliated Hospital to Xiamen Medical College                               |
| Zong'en Gao   | Department of Neurology                           | Shengli Oilfield Central Hospital  |
| Dongsheng Ju  | Department of Neurology                           | Songyuan Jilin oil Field Hospital  |
| Cunfeng Song  | Department of Interventional<br>Neuroradiology    | Liao Cheng the third people's hospital   |
| Jinggang Xuan | Department of Neurology                           | The First People's Hospital of Changzhou   |
| Feng Zhou     | Department of Neurology                           | Taiyuan Central Hospital   |
| Qing Shi      | Department of Neurology                           | Affiliated Jiangmen Traditional Chinese<br>Medicine Hospital of Ji'nan University      |
| Jun Luo       | Department of Neurology                           | Sichuan Mianyang 404 Hospital  |
| Yan Liu       | Department of Neurology                           | JingJiang People's Hospital, the Seventh<br>Affiliated Hospital of Yangzhou University |
| Zaiyu Guo     | Department of Neurosurgery                        | Tianjin TEDA Hospital  |
| Tong Li       | Department of Neurosurgery                        | The second Nanning People's Hospital   |
| Hongbo Zheng  | Department of Neurology                           | West China Hospital, Sichuan University  |
| Linzhi Dai    | Department of Neurosurgery                        | First Affiliated Hospital School of Medicine<br>Shihezi University                     |
| Junfeng Zhao  | Department of Neurology                           | Siping Central People's Hospital   |
| Liqiang Gui   | Emergency and Critical<br>Stroke Ambulance Center | Langfang Changzheng Hospital   |
| Xiaokun Geng  | Department of Neurology                           | Beijing Luhe Hospital, Capital Medical University                                      |
| Yufeng Tang   | Department of Neurology                           | Mianyang Central Hospital  |
| Congguo Yin   | Department of Neurology                           | Hangzhou First People's Hospital   |
| Hua Yang      | Department of Neurology                           | The affiliated Hospital of Guizhou Medical University                                  |

## Supplemental table 3. Registered Large infarct core volume thrombectomy trials

| Trial                            | TENSION                    | LASTE                                       | TESLA                 | RESCUE - Japan<br>LIMIT              | SELECT - 2   | ANGEL - ASPECT   |
|----------------------------------|----------------------------|---|-----------------------|--------------------------------------|--|--|
| NCT number                       | NCT03094715                | NCT03811769                                 | NCT03805308           | NCT03702413                          | NCT03876457  | NCT04551664  |
| Participating<br>Country(ies)    | Europe, Canada             | Europe, United States                       | United States         | Japan                                | United States, Canada,<br>Europe   | China  |
| Major imaging inclusion criteria | NCCT or DWI ASPECTS<br>3-5 | NCCT or DWI ASPECTS<br>0-5 (4-5 for > 80 y) | NCCT or ASPECTS 2 - 5 | CT ASPECTS 3-5 or DWI<br>ASPECTS 3-5 | 1. ASPECTS ≥6 and CTP core<br>≥50 cc<br>2. ASPECTS 3 - 5 and core<br>≥50 cc<br>3. ASPECTS 3 - 5 and core <50<br>cc | 1. ASPECTS 3-5<br>2. ASPECTS >5 (>6 h) and core<br>70-100 cc<br>3. ASPECTS <3 and core 70-<br>100 cc |

| Trial  | TENSION   | LASTE  | TESLA  | RESCUE - Japan<br>LIMIT  | SELECT - 2   | ANGEL - ASPECT  |
|--|---|--|--|--|--|---|
| NIHSS score  | <26   | >5   | >6   | ≥6   | ≥6   | 6 - 30  |
| Age, y   | >18   | ≥18  | 18 - 85  | >18  | 18 - 85  | 18 - 80   |
| Time window  | <12 h LSW   | <6.5 h LKW   | Random <24 h   | Random <6 h LKW, 6 - 24<br>FLAIR (-)   | Treat <24 h (0-12 vs 6-<br>24)   | Random <24 h  |
| Occlusion site                                     | Terminal ICA and<br>MCA M1  | Intracranial ICA, MCA<br>M1 or M1-M2   | Terminal ICA and M1  | Terminal ICA and M1  | ICA or MCA M1, tandem  | Terminal ICA and/or MCA M1<br>Tandem occlusion included   |
| Required time limit from randomization to puncture | No  | Yes<br>Randomization to<br>arterial access<br>30 min   | No   | Yes<br>Randomization to<br>arterial access<br>60 min   | No   | Yes<br>Randomization to arterial<br>access<br>60 min  |
| Bridging therapy<br>permitted                      | Yes   | Yes  | Yes  | Yes  | Yes  | Yes   |
| Intervention<br>model                              | EVT, no specified device  | EVT, no specified device   | FDA - approved EVT devices   | EVT, no specified device   | EVT with SR<br>Device: Trevo, Solitaire,<br>and EmboTrap   | EVT, IA - thrombolysis,<br>angioplasty<br>Device: Solitaire,<br>EMBOTRAP, Reco SR, Penumbra<br>aspiration catheter, or<br>CFDA - approved EVT devices |
| Major exclusion criteria                           | Mass effect on CT<br>Vascular disease<br>prevent MT (eg,<br>aortic dissection<br>or aneurysm, no<br>arterial<br>transfemoral<br>access) | Suspicion of aortic dissection, excessive tortuosity of cervical vessels on vascular imaging Multiple occlusion Cervical tandem lesion that requires stent placement | Refractory<br>hypertension<br>Mass effect on CT<br>Tandem lesion<br>Difficult<br>endovascular access<br>on vascular images | Mass effect on CT<br>Clinical evidence of<br>chronic occlusion<br>High risk of<br>hemorrhage (platelet<br><40,000/ µL,<br>APTT >50 s or PT-<br>INR >3.0) | Mass effect on CT<br>Inability to undergo CTA<br>and/or CTP<br>tPA 3-4.5 h<br>With special situation*<br>ICA dissection or aortic<br>dissection<br>Multiple occlusions | Refractory hypertension Mass effect on CT Multiple occlusions INR >1.7 or APTT >35 s; platelet count <100×10°/L                                       |
| Primary outcome                                    | mRS score shift analysis  | mRS score at 90 and<br>180 d   | Utility - weighted<br>90 - d mRS score   | mRS score 0 - 3 at 90 d  | Shift on 90 - d mRS score  | mRS score at 90 d   |
| Actual study<br>start date                         | July 20, 2018   | April 7, 2019  | July 16, 2019  | November 2018  | October 11, 2019   | September 28, 2020  |

Source: <a href="https://clinicaltrials.gov">https://clinicaltrials.gov</a>. ANGEL-ASPECT, Study of EVT in Acute Anterior Circulation LVO Patients with a largE infarCT core; Core: rCBF <30% on CT perfusion or ADC <620. ADC indicates apparent diffusion coefficient; APTT, activated partial thromboplastin time; ASPECTS, Alberta Stroke Program Early CT Score; CFDA, China Food and Drug Administration; CT, computed tomography; CTA, computed tomography angiography; CTP, computed tomography perfusion; DWI, diffusion-weighted imaging; EVT, endovascular treatment; FDA, US Food and Drug Administration; FLAIR, fluid-attenuated inversion recovery; IA, intra-arterial; ICA, internal carotid artery; INR, international normalized ratio; LASTE, Large Stroke Therapy Evaluation; LKW, last known well; LSW, last seen well; LVO, large vessel occlusion; MCA, middle cerebral artery; mRS, modified Rankin Scale; MT, mechanical thrombectomy; NCCT, noncontrast CT; NCT, National Clinical Trial; NIHSS, National Institutes of Health Stroke Scale; PT-INR, Pro-thrombin Time-International Normalized Ratio; RESCU-Japan LIMIT, Randomized Controlled Trial of Endovascular Therapy for Acute Large Vessel Occlusion With Large Ischemic Core; rCBF, relative cerebral blood flow; SELECT-2, Thrombectomy for Emergent Salvage of Large Anterior Circulation Ischemic Stroke; SR, stent retriever; TESLA, Thrombectomy for Emergent Salvage of Large Anterior Circulation Ischemic Stroke and tPA, tissue plasminogen activator.

<sup>\*(1)</sup> Age >80 y, (2) current anticoagulant use, (3) history of diabetes and prior stroke, (4) NIHSS >25, and (5) ischemic involvement of more than one-third of MCA territory.